Diseaese of RBCs

Dr. Maie Ismaiel
Cairo University

RED BLOOD CELL DISORDERS

RBC

- Life span: 120 days
- Count: 4.5 -5 million / cubic mm, males> females

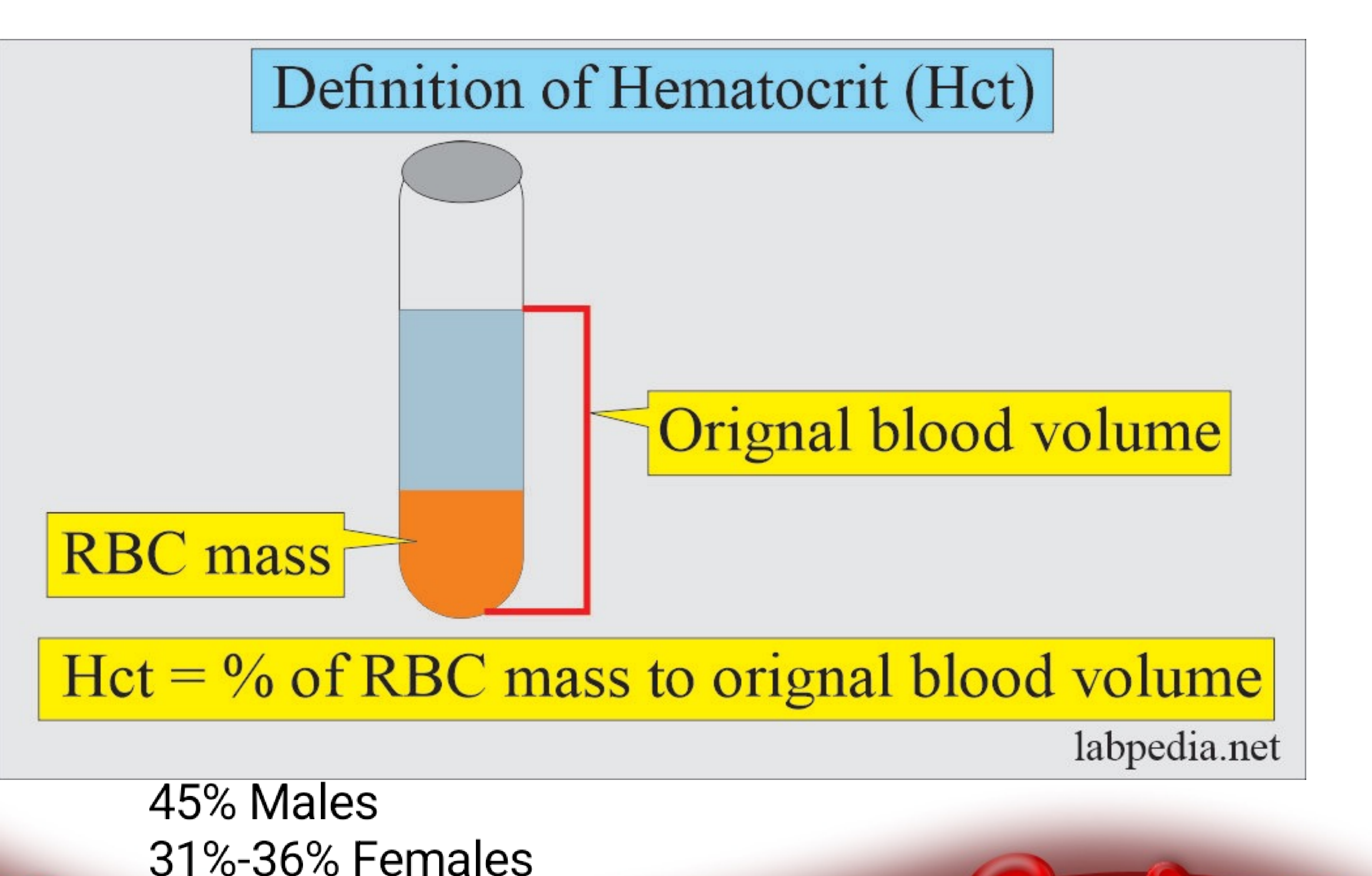
Hemoglobin:

- 13-16 gm/ dl in males
- 13-14 gm/ dl in females
- 12-13 gm/ dl in children



RBC disorders:

1. Polycythemia
2. Anemia



45% Males
31%-36% Females

DEFINITIONS:

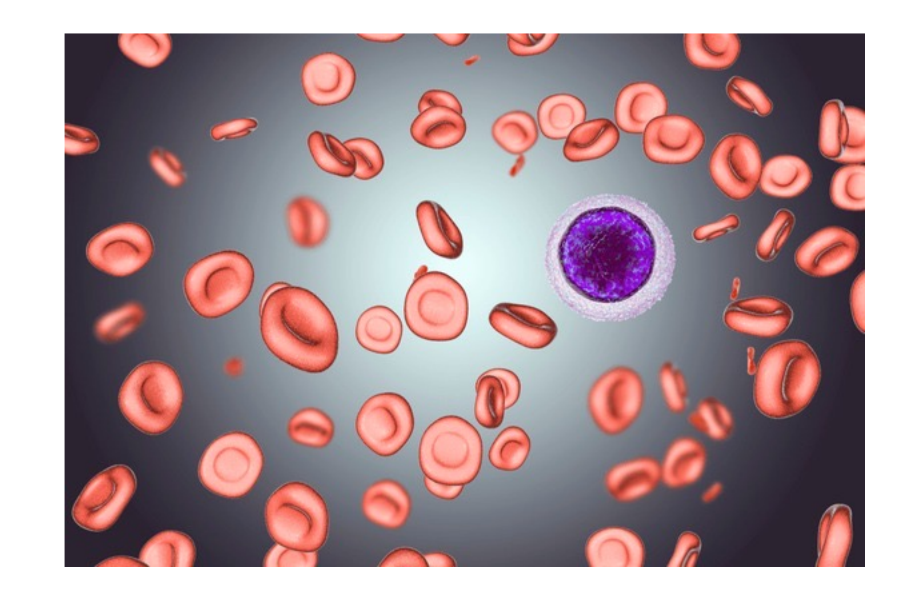
- **Mean cell volume** (MCV)
  - It is the measure of average volume of RBCs

for the cell volume itself (70-80 FL)

- **Mean cell Hemoglobin** (MCH)
  - It is a measurement of the average weight of hemoglobin in individual erythrocytes.
- **Mean Cell Hemoglobin Concentration** (MCHC)
  - It is the average concentration of hemoglobin in erythrocytes

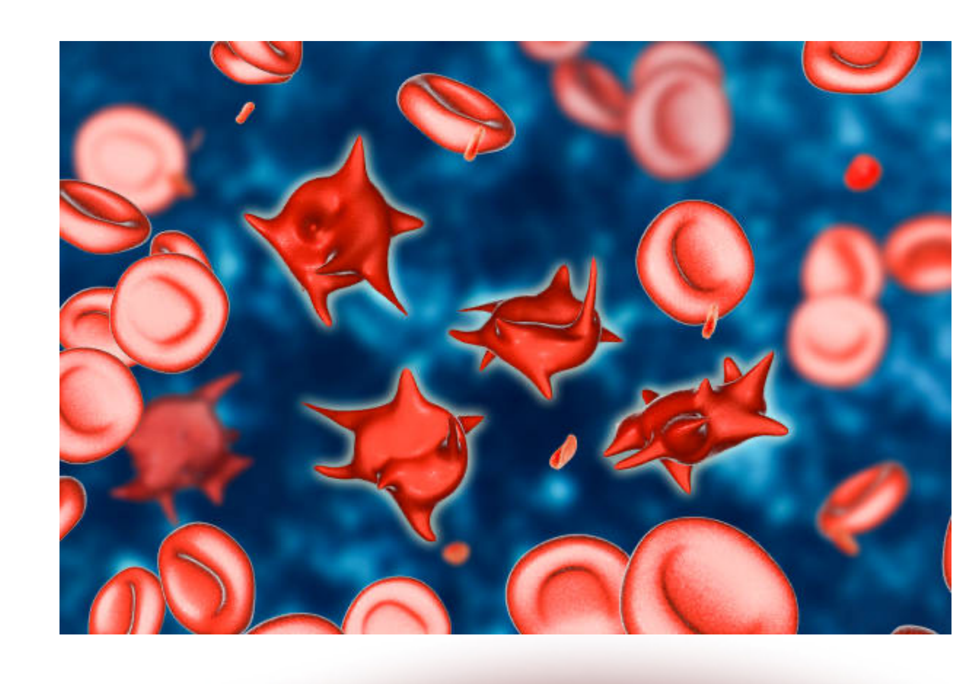
Anisocytosis

- Anisocytosis **describes red blood cells that are of different sizes.**
- Normal red blood cells are **generally the same size.** Having red blood cells of **unequal sizes may be a sign of anemia,**



POIKILOCYTOSIS

- Poikilocytosis refers to an **increase in abnormal red blood cells of any shape that makes up 10% or more of the total population.**
- Poikilocytes can be **flat, elongated, teardrop-shaped, crescent-shaped, sickle-shaped,**



Polycythemia

- Abnormal **increase in the erythrocyte count in the peripheral blood, usually accompanied by an increase in hemoglobin and hematocrit.**

- Polycythemia is divided into ***absolute*** erythrocytosis (a true increase in redcell mass) and ***relative*** erythrocytosis (the red cell mass is normal, but the plasma volume is reduced

Relative Polycythemia is caused by

1. Loss of tissue and intravascular fluid, which may be the result of such diverse conditions as **diabetic ketoacidosis, postsurgical dehydration, prolonged vomiting or diarrhea.**
2. Rapid diuresis secondary to treatment for congestive heart failure.

- In relative polycythemia, the hemoglobin rarely rises more than 25%, and there are no appreciable oral changes.

Absolute polycythemia is caused by

I- Primary (idiopathic) Polycythemia: "Polycythemia rubra vera".

- It is of unknown etiology, characterized by increase in all blood cells (RBCs, WBCs, platelets).

- it affects elderly patients and has slight male predominance.

Polycythemia

The essential disturbance of PC.RV includes:

1. Increased number of RBCs (may reach 18 million/mm"),
2. Increased hemoglobin (18-24 g/dl).
3. Bone replacement by erythropoietic tissue
4. Increased platelets count with platelets dysfunction in 50% of cases
5. Increased blood viscosity (mainly increased cell mass).
6. Decrease serum iron and ferritin.

Polycythemia

II. Secondary Polycythemia: "Erythrocytosis"

It is secondary to:

1. Congenital heart disease (right to left shunt).
2. Pulmonary disease.
3. Some tumors that release erythropiotin like substance (brain tumour).
4. People living in high altitude.

Polycythemia

Clinical features:

The main clinical problems are due to:

A. Increased blood volume.

B. Increased blood viscosity → thrombosis.

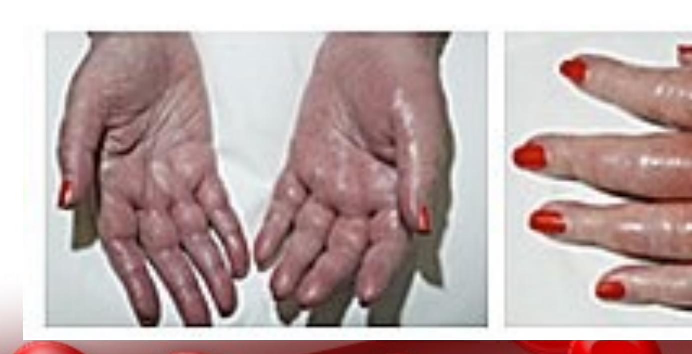
C. Bone marrow over activity

Polycythemia

Extra-oral features:

A. Purplish-red face and extremities.
B. Distended and dark superficial viens of neck.
C. Headache.
D. Spleenomegaly.
E. Bone pain, secondary to bone marrow hyperplasia.
F. Bleeding-bruising (petechiae & ecchymosis) or thrombosis as a result of platelets dysfunction and increased blood viscosity.



Polycythemia

Oral features:

A. Purplish-red oral mucosa.

B. Varicositis in the ventral aspect oftongue.

C. ***Bleeding from gingiva due to :***

- Increased number of platelets is accompanied by defective function.
- Dissiminated intravascular coagulation which consumes clotting factors.

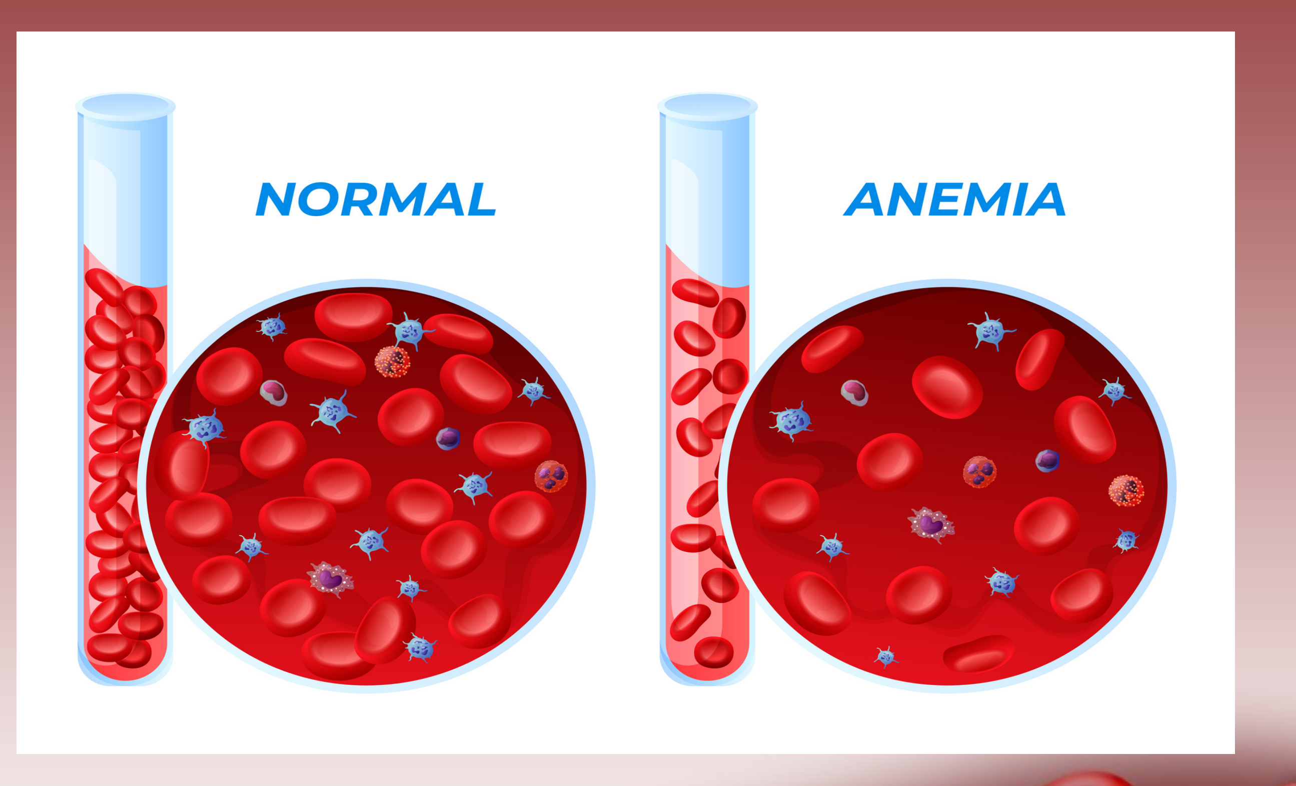
D- Petechia and ecchymoses.

Polycythemia

Dental management:

- Special attention to local hemostasis is required

Anemia



Anemia

Definition:

- Anemia is defined as reduction in the oxygen carrying capacity of the blood. It is usually related to decrease in the number of circulating red blood cells and reduction of the quantity of hemoglobin

MICROCYTIC

NORMOCYTIC

MACROCYTIC

MCV less than 80 fl

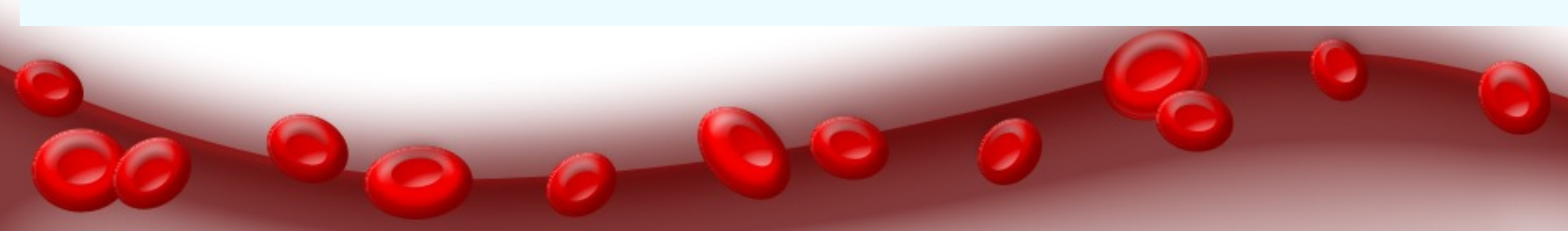
Small Red Blood Cell

MCV 80-100 fl

Normal Red Blood Cell

MCV greater than 100 fl

Large Red Blood Cell



Anemia

Classification of Anemia: may be classified according to:

The size of RBCs into:

- Normocytic, Microcytic and Macrocytic Anemia.

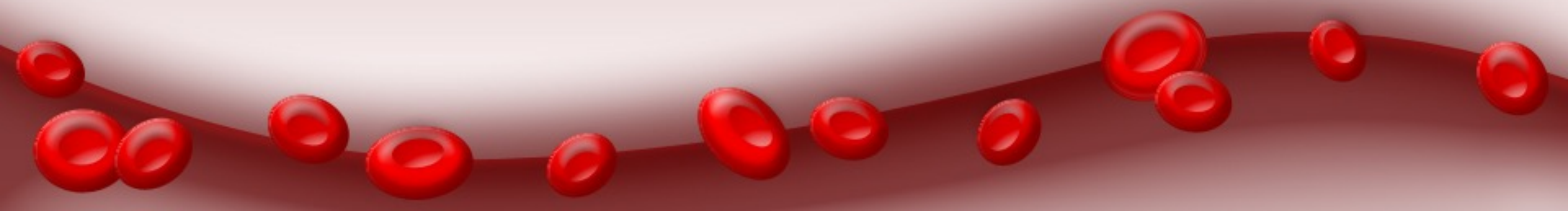
The hemoglobin concentration into:

- Hypochromic and Normochromic Anemia.

Anemia

There are three types of anemia

	MCV	MCH	MCHC	Disease
1. Normocytic	Normal	Normal	Normal	Aplastic anemia
2.Microcytic hypochromic	Decrease	Decrease	Decrease	Iron deficiency anemia
3.Macrocytic normochromic	Increase	Increase	Normal	Pernicious anemia Foliate deficiency anemia

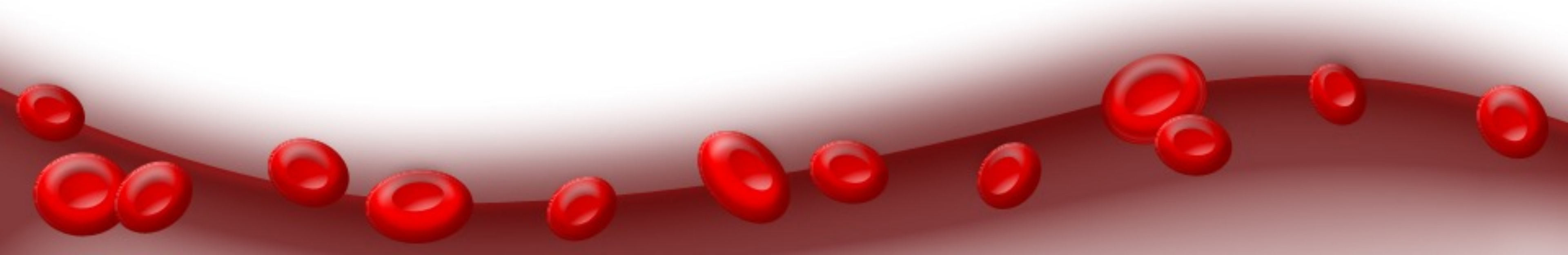


Iron Deficiency Anemia

Iron Deficiency Anemia

Definition

- Iron deficiency anemia is Microcytic Hypochromic anemia it is the most common type of anemia particularly in women of child bearing age



Anemia

Etiology of iron deficiency anemia:

- Increased blood loss
- Increased red blood cell destruction.
- Decreased red blood cell production
- Combination of the above.

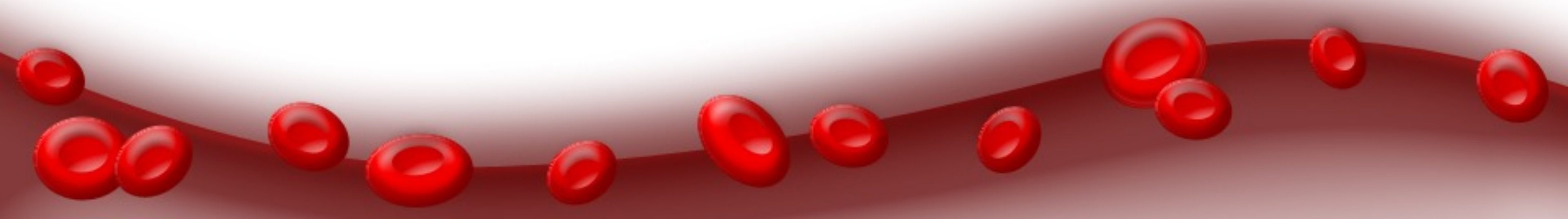
Iron Deficiency Anemia

Etiology:

1. Mainly due to chronic blood loss e.g. heavy menstruation.
2. Impaired iron absorption

   I. Gastrectomy (due to ↓ HCl)

   II. Consumption of tea with meals (tannic acid interfere with iron absorption)



Iron Deficiency Anemia

3. **Inadequate iron intake**

4. **Increased iron requirement e.g. pregnancy**

Clinical features:

1. Due to iron depletion
2. Due to anemia and tissue hypoxia (in all anemias)

Iron Deficiency Anemia

a) Symptoms

- Fatigue
- Headache
- Palpitation
- Dyspnea on exertion

b) Signs

- pallor of skin, nail beds & palpeberal conjunctiva.
- Tachycardia
- Cardiac murmurs
- Sparse hair
- Brittle nails,
- Koilonychia: spoon shaped and brittle nails

Oral Features:

a. Pallor of oral mucosa.

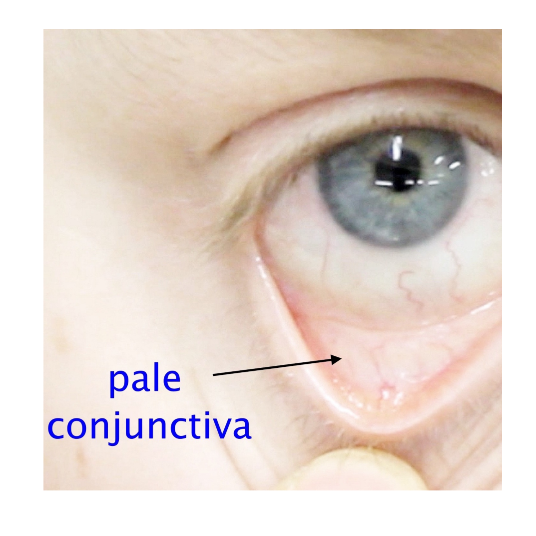
b. Angular cheilitis

c. Glossitis: sore atrophic tongue, in severe cases atrophy of filliform and fungifrom papillae and the tongue appears red atrophic.

d. Sore mouth: sore atrophic changes of oral mucosa.

e. Slow wound healing. Due to decreased iron storage. The epithelial integrity depends on adequate serum iron level.




pale
conjunctiva




(a)

Iron Deficiency Anemia

Diagnosis:

1. Case history.
2. Clinical examination.
3. Laboratory **investigations**:

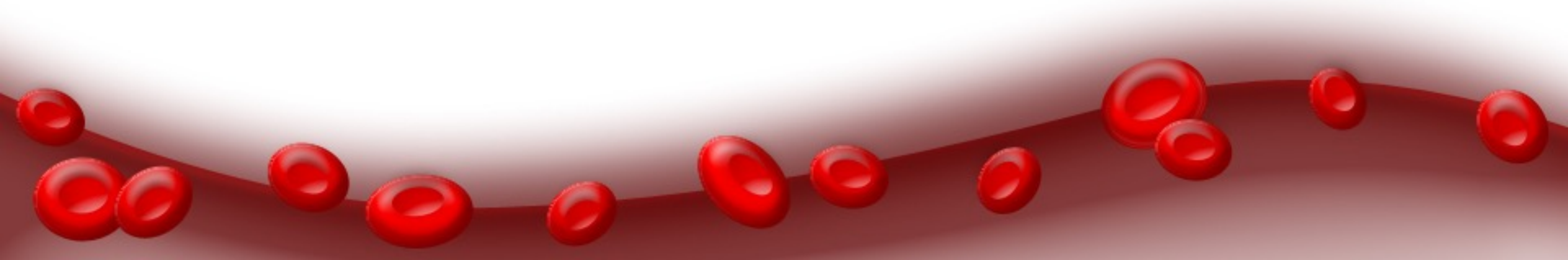
Iron Deficiency Anemia

- RBCs count. (3,000,000 - 4,000,000/mm3)
- Hb concentration (less than 11 g/dl of blood)
- MCV, MCH, MCHC
- Serum ferritin levels <25 mcg/L are highly suggestive of IDA, while levels >100mcg/L are reflective of good iron stores.
- Many immature cells are seen in peripheral blood
- RBC may be irregular in size (anisocytosis) or irregular in shape (poikilocytosis).

Iron Deficiency Anemia

Treatment

- The cause of iron deficiency should be identified and eliminated.
- Ferrous sulphate or ferrous gluconate tablets (325mg three times per day) best absorbed when the patient is fasting.



Iron Deficiency Anemia

Dental Implication

- CBC with differential should be ordered for anemic patient.
- Avoid surgical procedures in severely anemic state because of increased bleeding & impaired wound healing.
- Avoid G.A if Hb < 10mg/dl

Plummer-Vinson Syndrome

Plummer-Vinson Syndrome

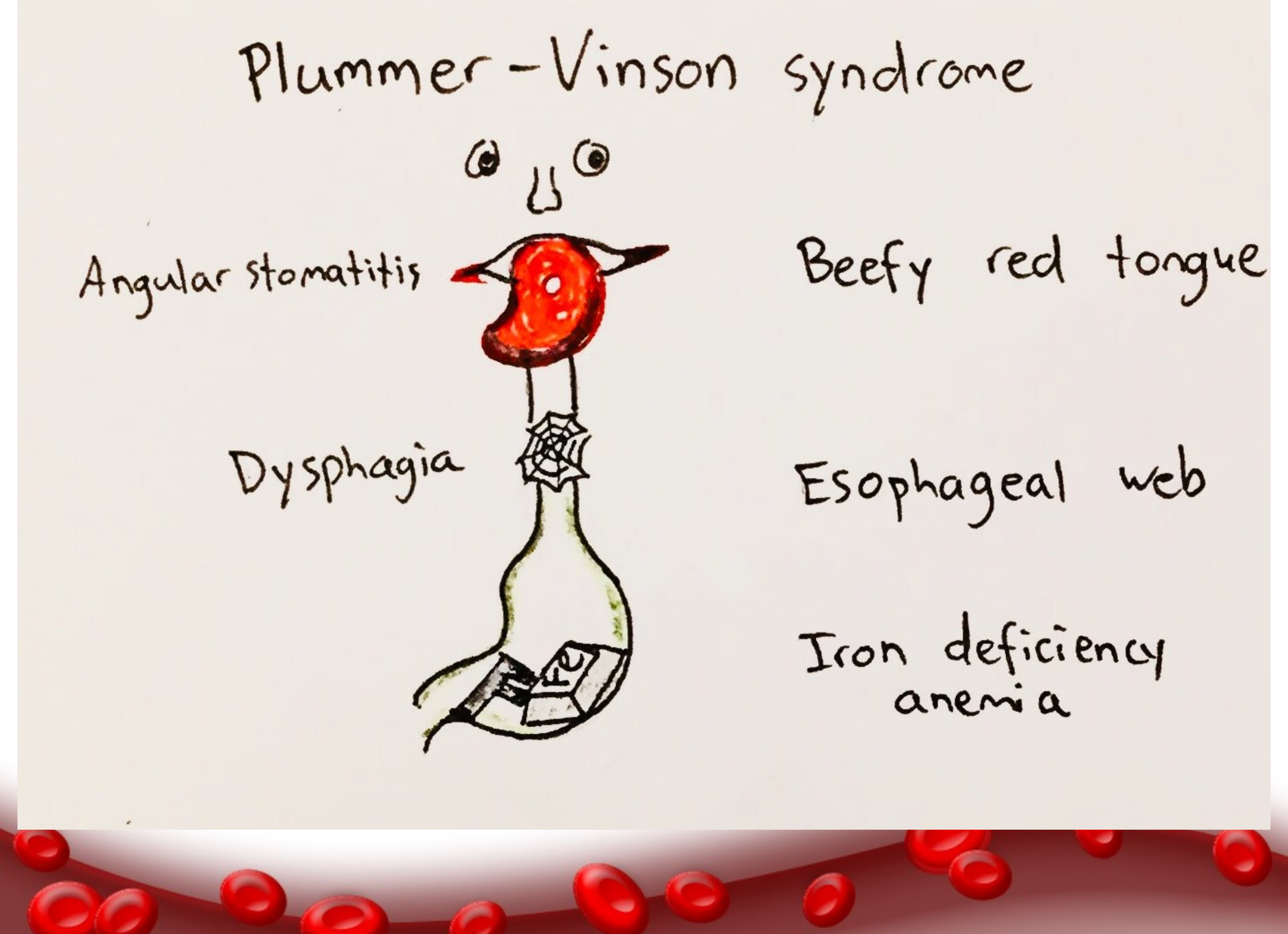
(Patterson-Kelley Syndrome)

- Plummer-Vinson syndrome is one manifestation of iron deficiency anemia.
- Plummer-Vinson syndrome is defined by the **classic triad of dysphagia, iron-deficiency anemia and esophageal webs.**
- Even though the syndrome is very rare nowadays, its recognition is important because it identifies a group of patients at increased risk **of squamous cell carcinoma** of the pharynx and the esophagus.

Plummer-Vinson Syndrome

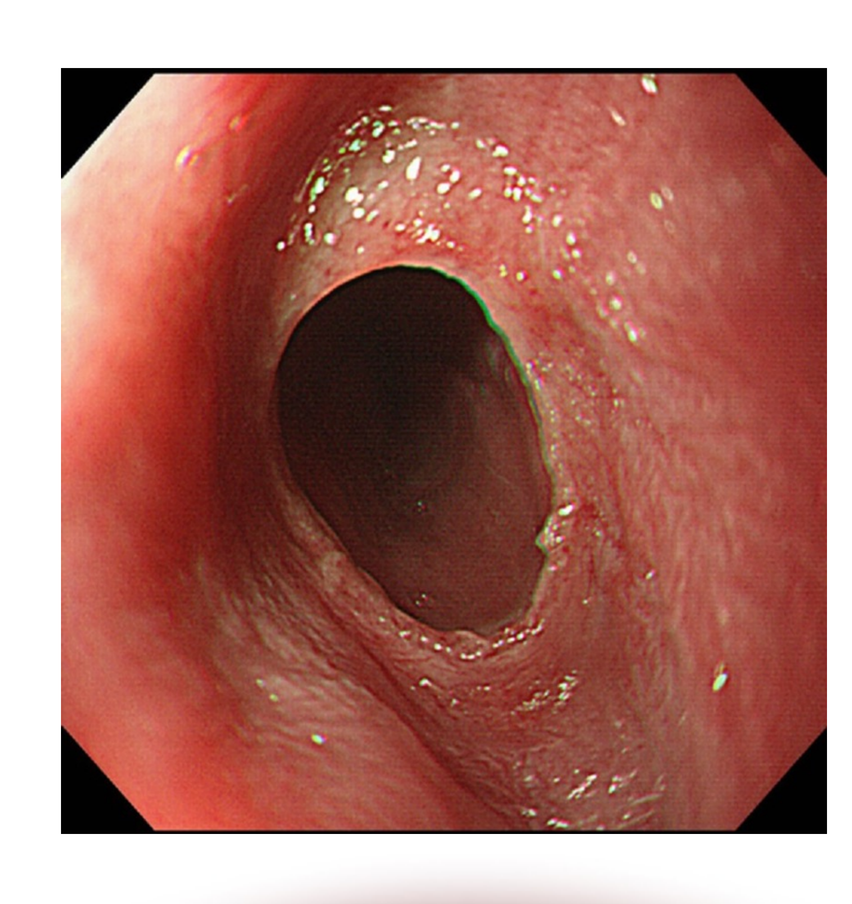
Plummer Vinson syndrome is characterized by:

1. Smooth red painful tongue with atrophy of filiform papilla and later by the fungiform papillae.
2. Atrophy of the mucosa of the mouth. Pharynx and upper esophagus.
3. Angular cheilitis and oral ulceration.
4. Dysphagia due to muscular degeneration of the esophagus and stenosis of the esophageal mucosa.



Plummer-Vinson syndrome
Angular stomatitis
Beefy red tongue
Dysphagia
Esophageal web
Iron deficiency anemia
Fe

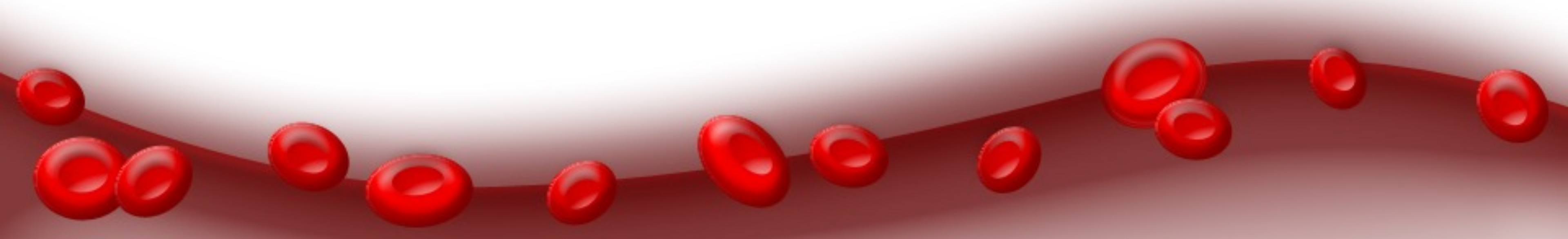
- An esophageal web is a thin (2-3 mm), eccentric, smooth extension of normal esophageal tissue consisting of mucosa and submucosa that can occur anywhere along the length of the esophagus but is typically located in the anterior postcricoid area of the proximal esophagus.



Plummer-Vinson Syndrome

- The depletion of iron stores in the body may be the direct **cause of mucosal atrophy**, since the integrity of the epithelium is dependent upon adequate serum iron levels.

- Patients with these syndromes should be followed up closely for any oral or pharyngeal changes that may be an early indicator of carcinoma

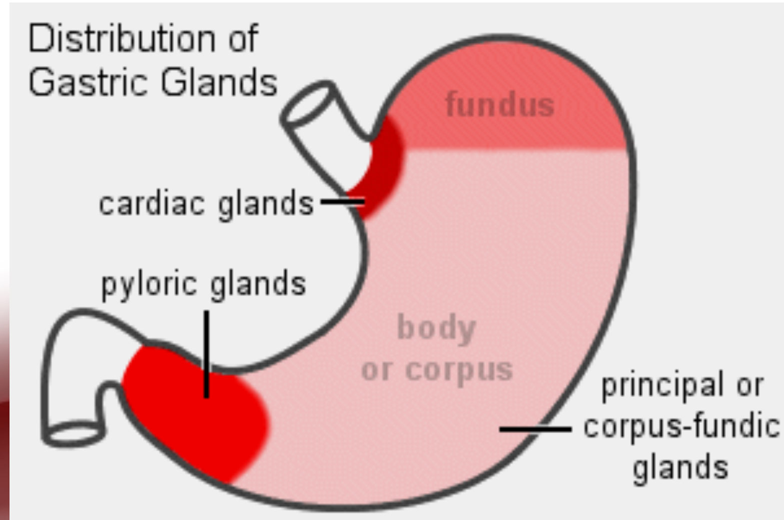


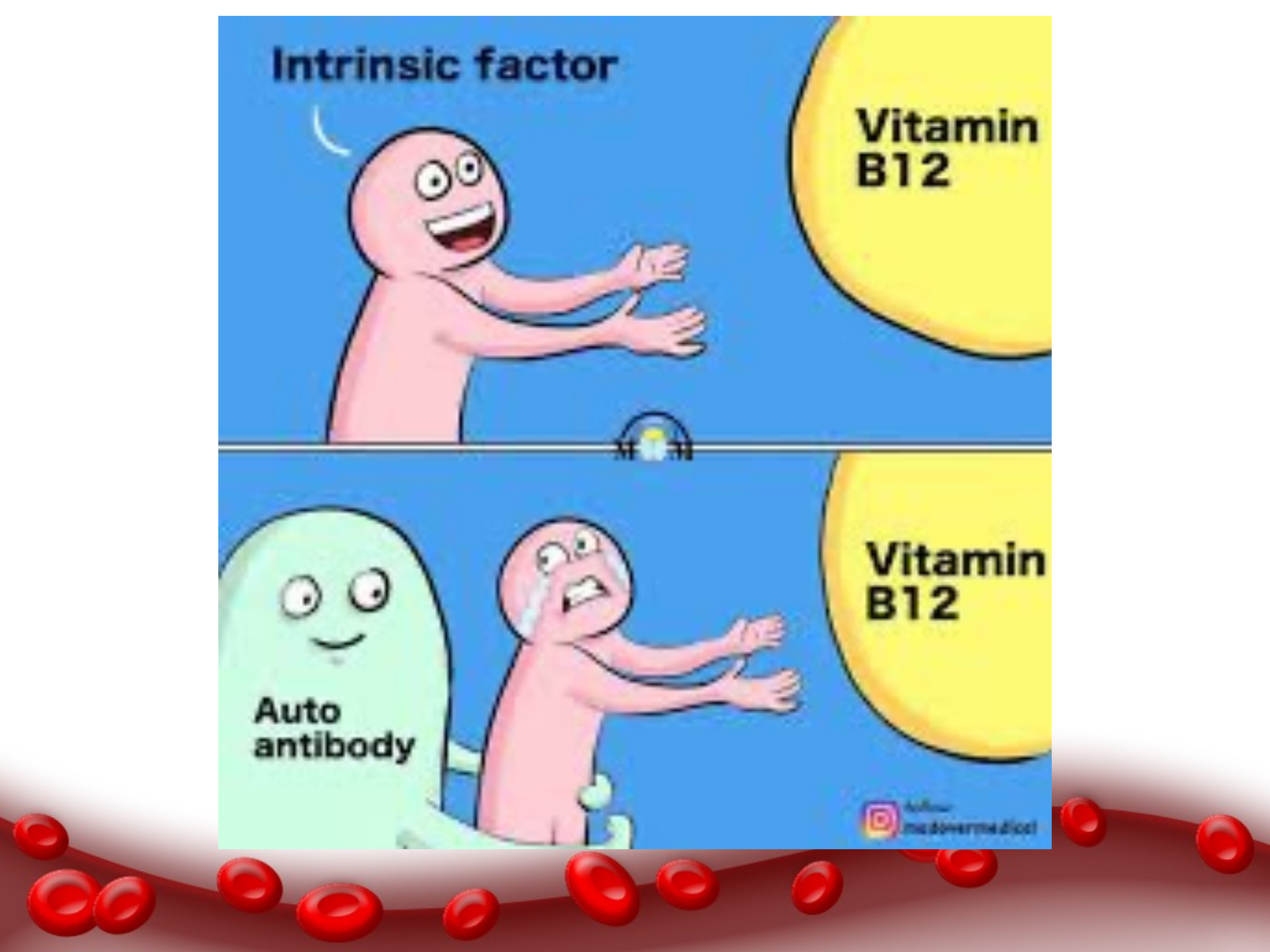
Pernicious Anemia (Addisonian Anemia)

Pernicious Anemia (Addisonian Anemia)

(Macrocytic Normochromic anemia)

- Is an autoimmune disease in which there is progressive destruction of the gastric fundic glands, leading to atrophic gastritis, loss of production of intrinsic factor and vitamin B12 malabsorption




Intrinsic factor
Vitamin B12
Vitamin B12
Auto antibody

Pernicious Anemia (Addisonian Anemia)

Etiology

- Circulating autoantibodies against parietal cells of stomach → ↓ in intrinsic factor secreted by parietal cells defect in vit. B12 absorption → defect in RBCs maturation → pernicious anemia.

Autoantibodies

- An autoantibody is an antibody produced by the immune system that is directed against one or more of the individual's own proteins. Many autoimmune diseases are associated with such antibodies.



Pernicious Anemia (Addisonian Anemia)

N.B.:

Vit. B12 is essential for:

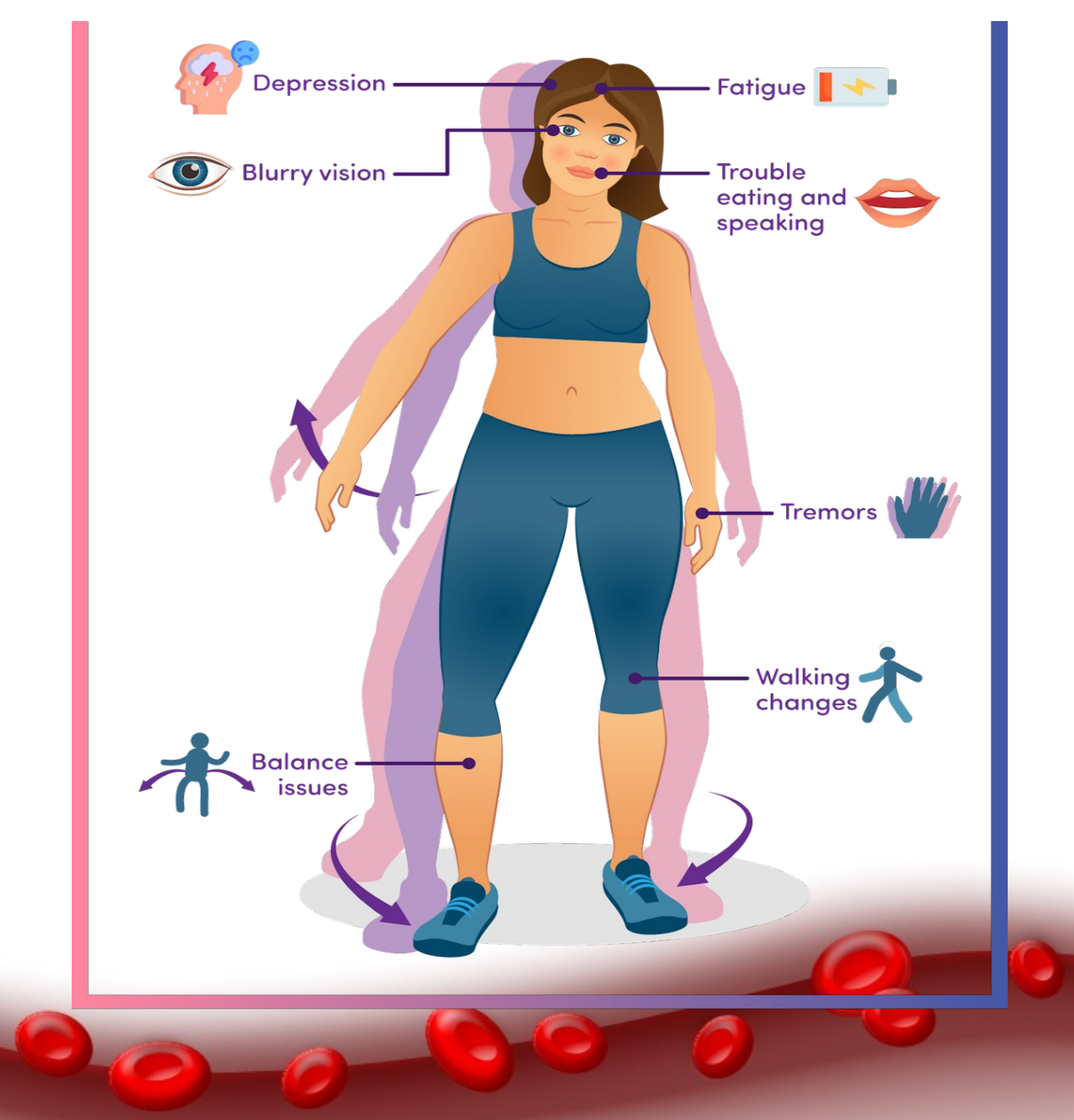
1. Maturation of RBCs
2. Metabolism of nerve tissues.

Vit. B12 deficiency results in:

1. ↓ Count of RBCs anemia.
2. Subacute combined degeneration of spinal cord causing neurologic manifestation.

Subacute combined degeneration of spinal cord

- Subacute combined degeneration is characterized by **degeneration of the dorsal columns and the lateral columns** of the spinal cord due to demyelination.
- It commonly presents with sensory deficits, paresthesia, weakness, ataxia, and gait disturbance.
- In severe untreated cases, it can lead to spasticity and paraplegia.



Depression
Fatigue
Blurry vision
Trouble eating and speaking
Tremors
Walking changes
Balance issues

Pernicious Anemia (Addisonian Anemia)

Clinical Features:

1. Insidious onset with progressive increasing sign and symptoms of anemia
2. Patient may show severe pallor (lemon yellow color) which is ***due to both:***

A. Tissue hypoxia.

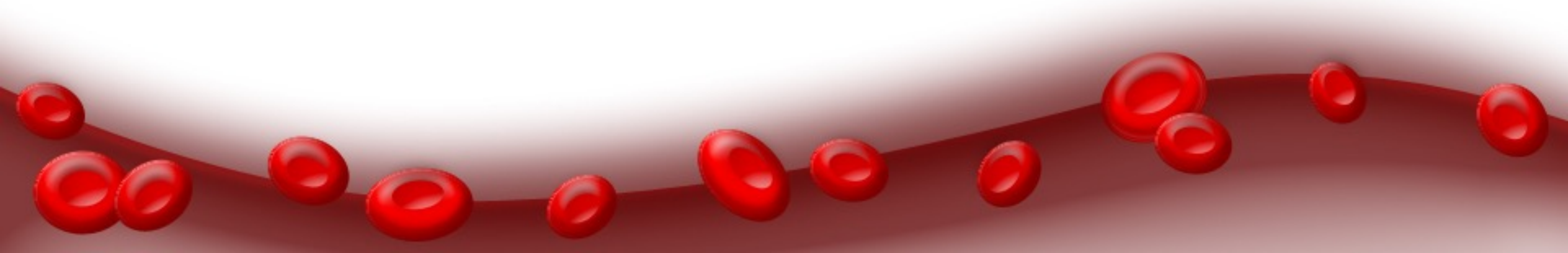
B. Jaundice: as a result of increased serum bilirubin due to premature breakdown of newly formed RBC in the bone marrow

- Jaundice, also known as hyperbilirubinemia, is defined as a yellow discoloration of the body tissue resulting from the accumulation of excess bilirubin. Deposition of bilirubin happens only when there is an excess of bilirubin, and this indicates increased production or impaired excretion.



On average, total bilirubin levels between 0.2 and 1.3 mg/dL are considered normal for children and adults.

Total protein		
Albumin		
Globulin		
Total bilirubin	25.2 H	mg/dL
Direct bilirubin	20.5 H	mg/dL
AST		U/L
ALT		U/L
ALP		U/L



Pernicious Anemia (Addisonian Anemia)

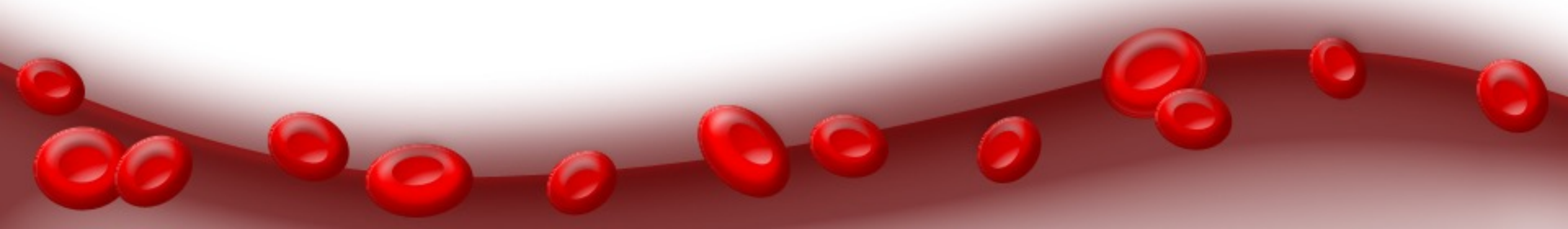
3. Neurological symptoms: develop in about 10% of cases. The patients suffer symmetrical numbness or tingling of the extremities, muscular weakness and ataxia.

4. Gastrointestinal symptoms: constipation, or diarrhea, vague epigastric pain and there is increased risk of stomach cancer

Pernicious Anemia (Addisonian Anemia)

Oral features

1. Glossitis, glossodynia & sore atrophic tongue
2. Pallor of the mucous membrane of the entire oral cavity.
3. Aphthous ulceration may occur particularly on the tongue.
4. The patient can't tolerate to wear the denture due to changes in oral mucosa.
5. Disturbance of taste sensation and a decrease in salivation, eventually xerostomia; may result



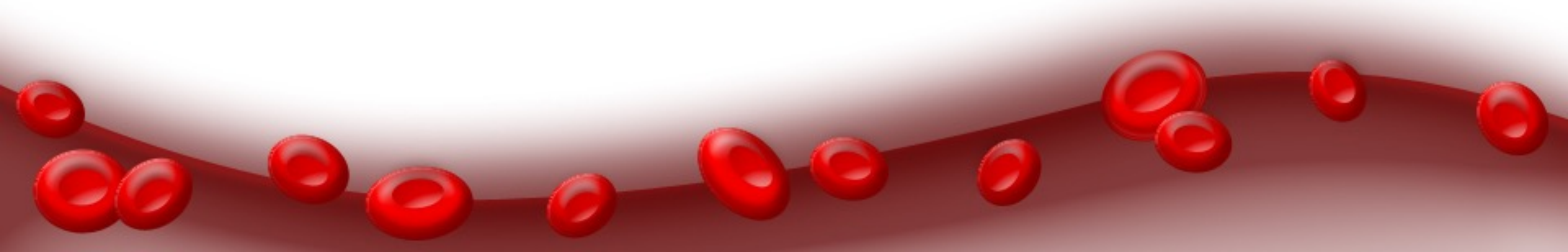

A
B

Pernicious Anemia (Addisonian Anemia)

Diagnosis:

A. The diagnosis of PA could be suspected if the patient complains of triad of symptoms:

1. Sore, painful atrophic tongue.
2. Generalized weakness
3. Numbness or tingling in the extremities



Pernicious Anemia (Addisonian Anemia)

b) Hematological finding

- ↓ RBCs count.
- ↓ Hb concentration.
- ↑ MCV, MCH
- Normal MCHC
- ↓ Serum vit. B t2 level (usually less than 100 pg/ml),

Pernicious Anemia (Addisonian Anemia)

c) Definitive diagnosis can be reached by

1. Schilling test:

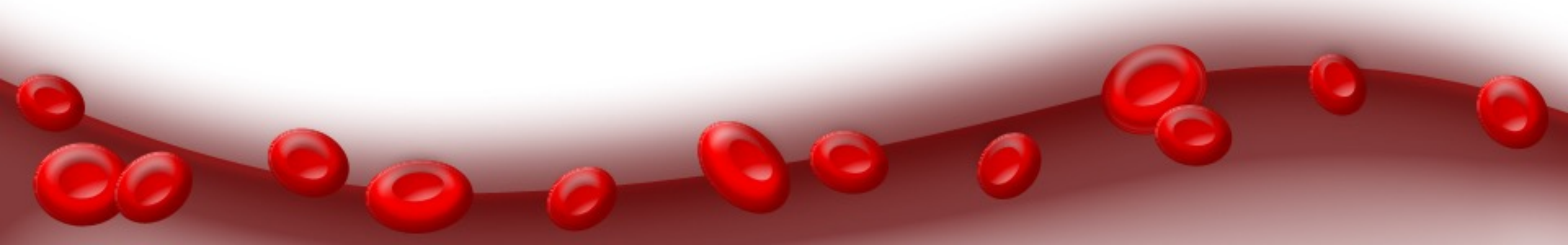
- Radiolabelled Vit. B 12 (small measured dose) given orally.
- Unlabelled Vit. B 12 (large dose) given 1M 1 or 2 hour later.
- Collect 24 hour urine.



Pernicious Anemia (Addisonian Anemia)

- Normal person can excrete >15% radio-labelled vit. B12 in PA it is less than 15% in 24 hours.

- **Repeat with added oral intrinsic factor. In PA:** excretion of vit. B12 increases to normal, while in presence of Celiac disease: excretion of vit. B12 remains low.



Pernicious Anemia (Addisonian Anemia)

2. Detection of serum antibody against

- Parietal cells which are found in 90% of cases.
- Gastric intrinsic factors are found in 60% of cases.

Treatment:

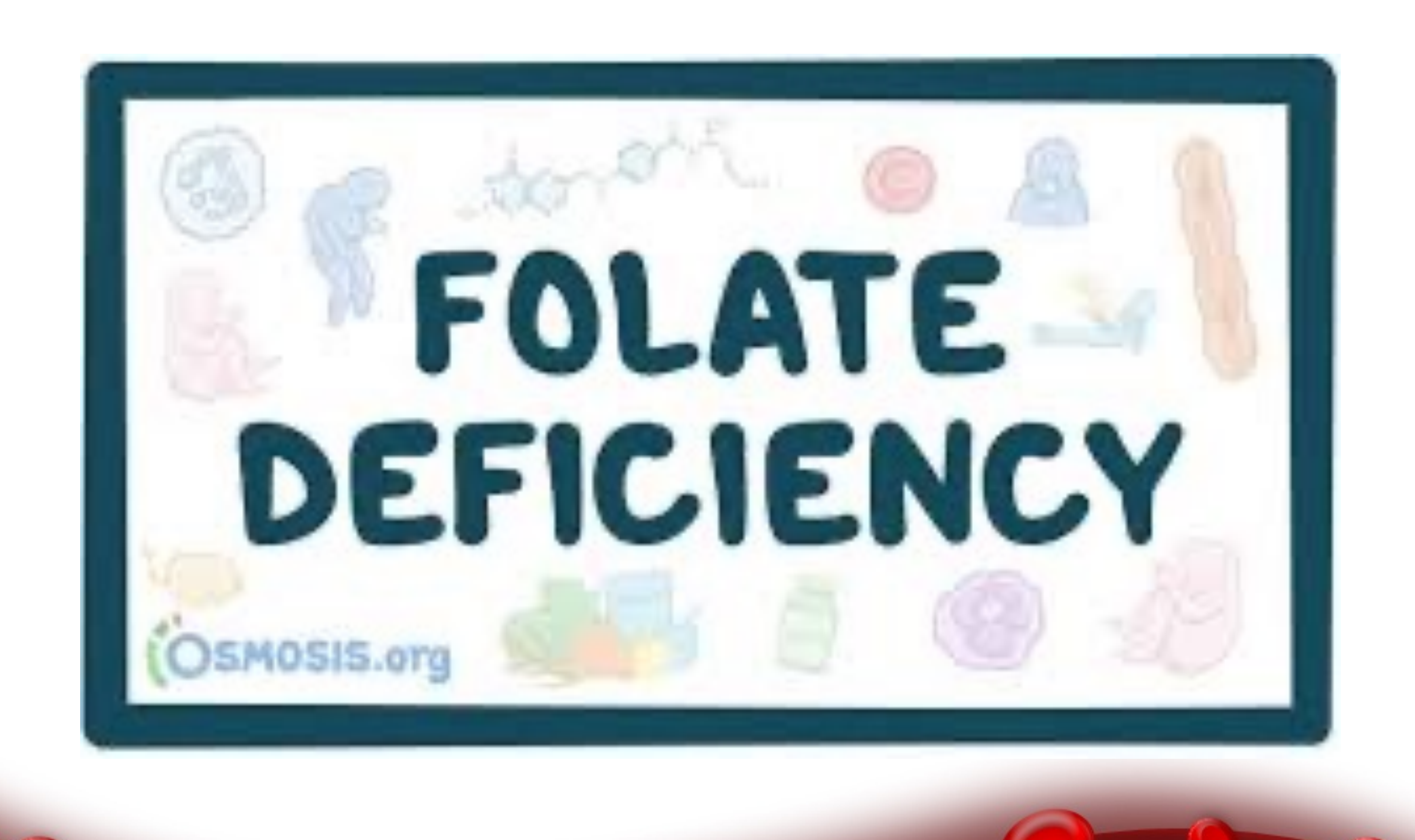
- Patients are treated (for life) with I.M. injection of hydroxy cobalamine (1000 µg), given as total dose of 5000-6000 µg over 3 weeks and then 1000 µg every three months.

Pernicious Anemia (Addisonian Anemia)

N.B.

- The hematological changes of pernicious anemia **may be improved by oral folic acid** therapy ***but will not stop the progression of neurologic symptoms***. It may aggravate neuropathy.

- For this reason anemic patients should never take folic acid therapy without being first sure that their anemia is not pernicious. Folic acid improves Hb level but the neurologic changes caused by PA continue to progress


FOLATE
DEFICIENCY
OSMOSIS.org

Folate Deficiency Anemia

- It is a **macrocytic normochromic anemia** due to deficiency of folic acid.

- ***The effects*** of folate and Vit. B 12 deficiency are similar, both cause ***Megaloblastic*** changes in the bone marrow and ***Macrocytic*** anemia.

- Unlike Vit B12 the body reserve of folate in the liver can be depleted within 4 months.

Folate Deficiency Anemia

The main causes of Folate deficiency are:

1. Poor intake.
2. **Malabsorption:** inflammatory bowel disease.
3. **Increased demand:** infancy, pregnancy, increased hemolysis
4. **Drugs:** alcohol, barbiturates, phenytoin and oral contraceptive pills.

Folate Deficiency Anemia

- The initial clinical presentation of folate and Vit.B12 deficiency may be indistinguishable from each other but , folate deficiency does not lead to neurological manifestation

Folate Deficiency Anemia

Folate deficiency anemia is characterized by:

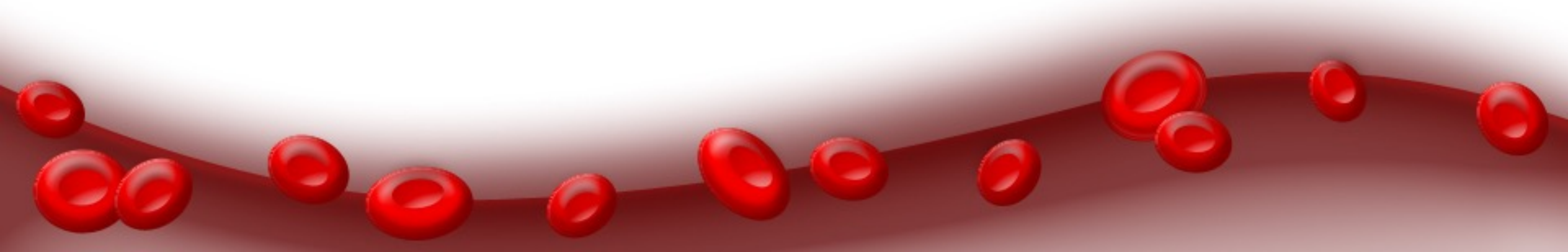
A. Serum folate level low and serum Vit.BI2 normal
B. Schilling test is normal.

Treatment:

- Folic acid 5 mg/daily

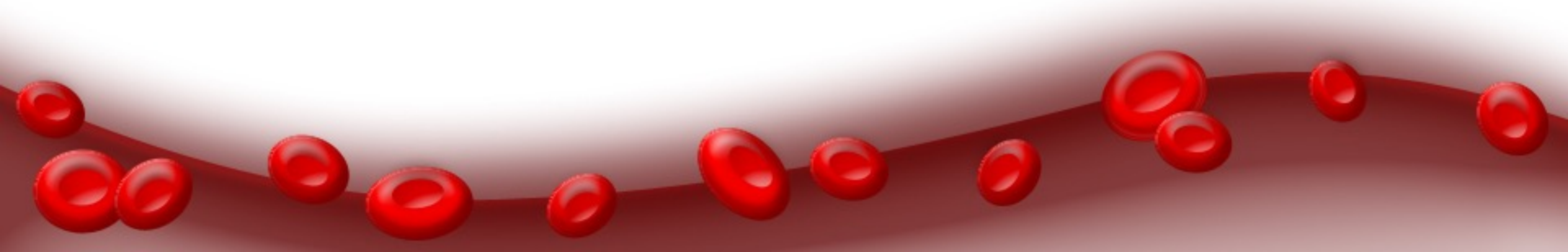
Glucose-6-Phosphate Dehydrogenase Deficiency

- G6PD deficiency is inherited as an *X-linked hemolytic anemia* caused by mutations in the G6PD gene.
- The WHO classifies the different variants according to the magnitude of enzyme deficiency and severity of hemolysis:
  - Class I is <1% of enzyme activity;
  - Class II is <10%,
  - Class III is 10%–60%,
  - Class IV is 60%–90%, and
  - Class V is >110%



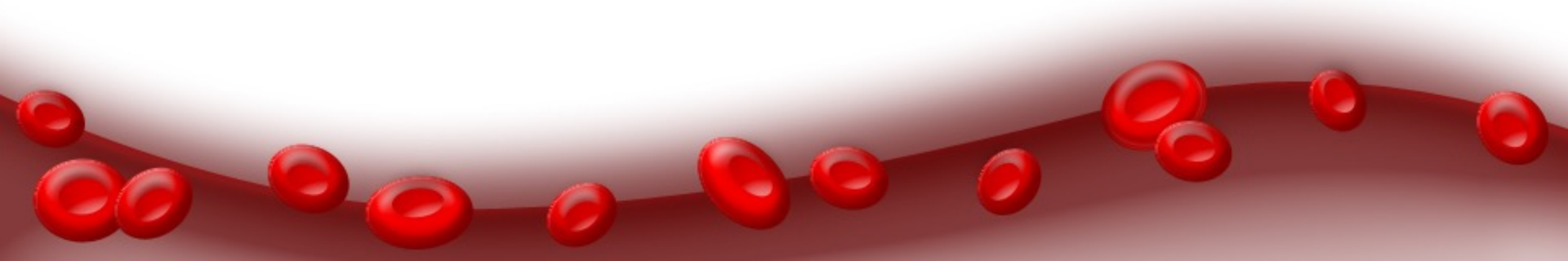
Glucose-6-Phosphate Dehydrogenase Deficiency

- **Clinical Manifestations:**
- The vast majority of individuals with G6PD deficiency remain clinically asymptomatic throughout their lives. If hemolysis occurs in an affected patient, characteristic signs and symptoms of fatigue, flank pain, anemia, and jaundice are evident.
- Triggers of crisis:
  - Ingestion of fava beans is a recognized trigger.
  - Infection is likely the most common trigger of hemolysis in at-risk.
  - Drugs



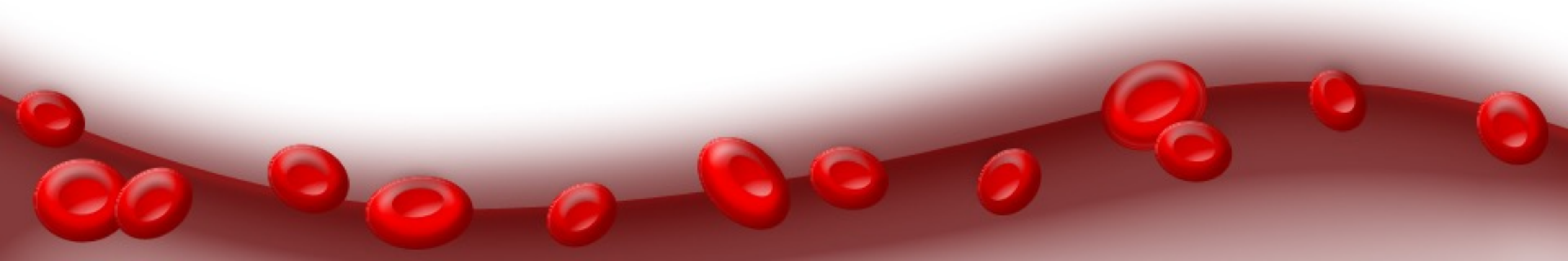
Glucose-6-Phosphate Dehydrogenase Deficiency

- Drug-induced hemolysis typically occurs within 24 to 72 hours of exposure and dark urine due to hemoglobinuria is characteristic.
- The anemia progresses for about a week, followed by recovery over the next 8 to 10 days.
- These includes:
  - Dapsone, methylene blue, toluidine blue, aspirin, vit K, probenecid, prilocaine, phenazopyridine primaquine, and most of sulphonamide.



Glucose-6-Phosphate Dehydrogenase Deficiency

- Oral Health Considerations:
  - Patients with G6PD deficiency can tolerate the delivery of all necessary dental care.
  - Medications known to induce a hemolytic crisis should be strictly avoided and oral infections should be promptly managed.
  - G6PD patients should maintain excellent oral hygiene and comply with routine recall visits so as to prevent oral and periodontal infection.





Aplastic Anemia

Aplastic Anemia

(Normocytic Normochronic Anemia)

- Aplastic anemia is a rare bone marrow aplasia, causing refractory ***Normocytic Normochromic*** anemia, leukopenia and thrombocytopenia (pancytopenia).

Aplastic Anemia

Etiology may be attributed to:

1) Primary:

A. **Congenital e.g.** Fanconi's anemia with features of skeletal, renal and CNS abnormalities.

B. **Acquired:** may be due to immune suppression of bone marrow stem cells by T suppressors cells.

FANCONI ANEMIA

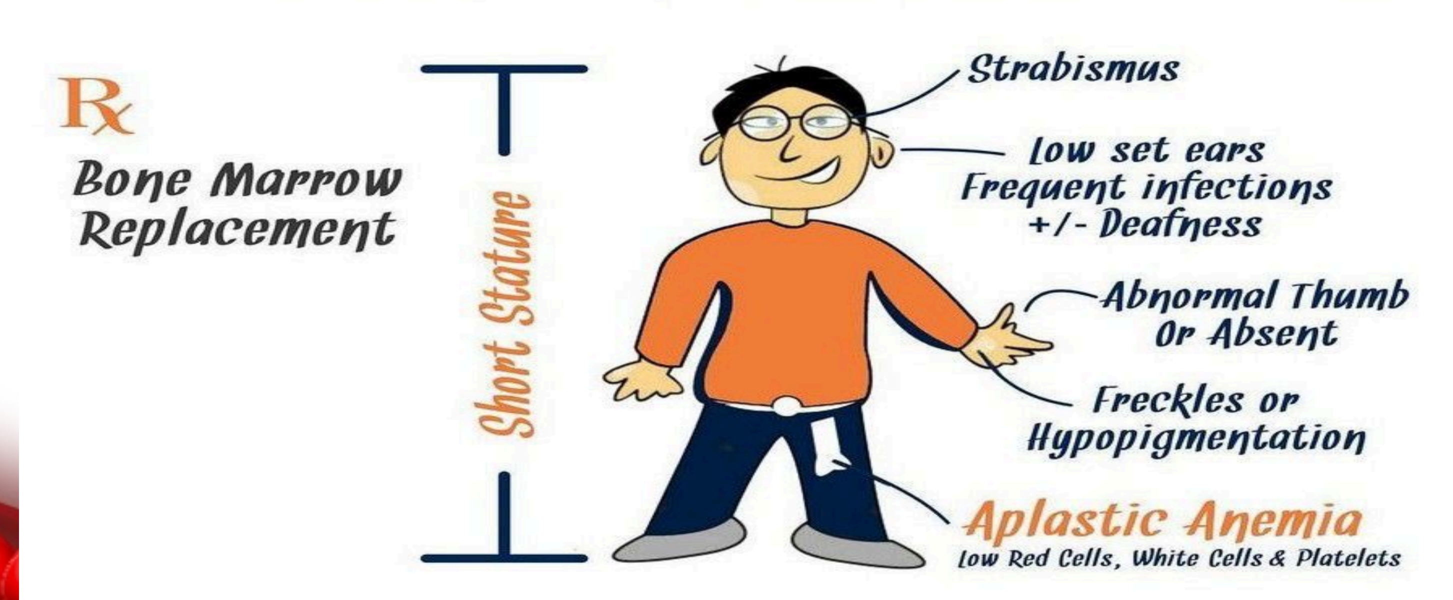
Fanconi anemia (FA) is an inherited bone marrow failure syndrome characterized by pancytopenia, predisposition to malignancy, and physical abnormalities, including malformations belonging to the VACTERL-H association.

Autosomal Recessive Genetic Disease

90% Develop Bone Marrow Failure by Age 40.

About 60-75% of People Have Congenital Defects

The Majority Develop Acute Myelogenous Leukemia



Aplastic Anemia

2) Secondary to:

Drugs: cytotoxic (busulphan) and noncytotoxic (chloramphinicol).

- ***Chemical:*** Ionizing radiation.
- ***Viral infection:*** vital hepatitis and measles.

Aplastic Anemia

Clinical Manifestations

- General features of anemia due to ↓RBCs…… ; Pallor
- Petechia, ecchymosis and bleeding due to ↓platelets.
- ***The oral manifestations include:***

Aplastic Anemia

1) Pallor of the oral mucosa,
2) Minimal but persistent gingival bleeding,
3) Petechiae and ecchymosis
4) Oral ulcers: large, deep, irregular **with no erythema around the ulcer** due to ↓ WBCs.
5) Increased risk of oral cancer





Aplastic Anemia

Diagnosis:

(1) Case history:

- History of drug intake as chloramphenicol.
- History of irradiation.

(2) Clinical examination.

(3) Laboratory investigation:

Aplastic Anemia

*** Pancytopenia: Decrease in the count of:**

- RBCs.
- Platelets.
- WBCs.

*** Normal**

- MCV, MCH & MCHC.

Aplastic Anemia

Treatment:

- Remove the cause if possible.
- Bone marrow transplant

Computer Software

real lab system

HEMATOLOGY REPORT

Blood Picture:

Reference Ranges :



Yash M. Patel



Sample Collected At:

Ref. By: Dr. Hiren Shah

Complete Blood Count (CBC)

Investigation | Result | Reference Value



Medical Lab Technician



Dr. Payal Shah

Dr. Vimal Shah





Clinical Information / Comments:

STOOL SAMPLES TO FOLLOW
SDRC,SOB FCAL SAMPLE NOT PASS
ACCEPTED AS PER PATIENT REQUEST

Requesting Physician : Zaigham Abbas
Account # : 109490173 - CLI
Requested on : 01/09/2020 - 18:42
Collected on : 01/09/2020 - 18:42
Reported on : 02/09/2020 - 04:52

Test	Result	Normal Ranges
[COMPLETE BLOOD COUNT]		
[HAEMOGLOBIN HAEMATOCRIT]		
HAEMOGLOBIN	10.9 g/dl	(11-14.5)
HAEMATOCRIT	34.8 %	(34.5-45.4)
R.B.C.	5.53 x10E12/L	(3.61-5.2)
M.C.V.	62.9 fL	(78.1-95.3)
M.C.H.	19.7 pg	(25.3-31.7)
M.C.H.C.	31.3 g/dL	(30.3-34.4)
R.D.W	14.6 %	(12.1-16.9)
W.B.C.	7.0 x10E9/L	(4.6-10.8)
NEUTROPHILS	47.8 %	(34.9-76.2)
LYMPHOCYTES	42.1 %	(17.5-45)
EOSINOPHILS	1.0 %	(0.3-7.4)
MONOCYTES	8.5 %	(3.9-10)
BASOPHILS	0.6 %	(0-1)
Neutrophils lymphocytes ratio (NLR)	1.1 ratio	(1-4)
PLATELETS	236 x10E9/L	(154-433)

METHODOLOGY:
The test is performed on Automated Haematology Analyzer.

PERIPHERAL FILM

ANISOCYTOSIS, HYPOCHROMIC, MICROCYTIC
POIKILOCYTOSIS, POLYCHROMASIA
ELLIPTICAL CELLS, TARGET CELLS
? THALASSEMIA MINOR
SUGGEST HEMOGLOBIN VARIENT ANALYSIS BY HPLC OR HB ELECTROPHORESIS

Kindly Note reference Ranges change on 06/12/2018.

This is a computer generated report therefore does not require any signature.

Dr. Bushra Moiz
MBBS, FCPS(Hematology)
Associate Professor

Dr. Mohammad Usman Shaikh
MBBS, FCPS(Hematology)
Associate Professor

Dr. Salman Naseem Adil
MBBS, FCPS (Hematology)
Professor

Dr. Natasha Ali
MBBS, FCPS (Hematology)
Associate Professor

Dr. Muhammad Shariq Shaikh
MBBS, FCPS (Hematology)
Assistant Professor

Dr. Anila Rashid
MBBS, FCPS(Hematology)
Assistant Professor

Dr. Muhammad Hasan
MBBS, FCPS(Hematology)
Senior Instructor

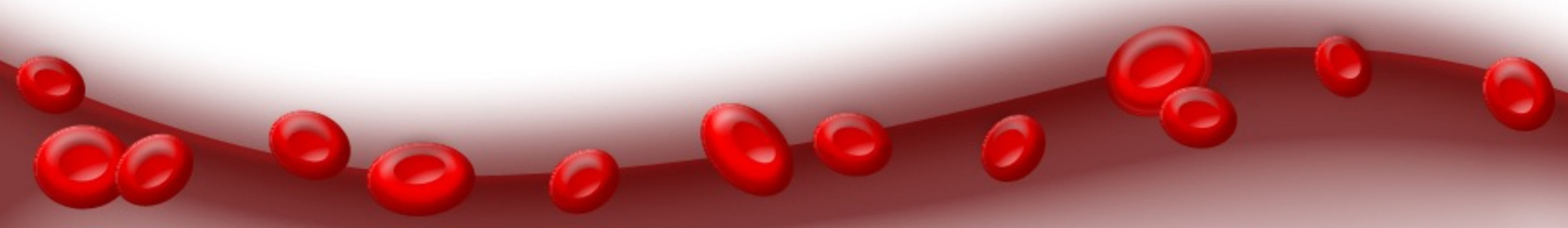
Definition of Hematocrit (Hct)

Orignal blood volume

RBC mass

Hct = % of RBC mass to orignal blood volume

labpedia.net



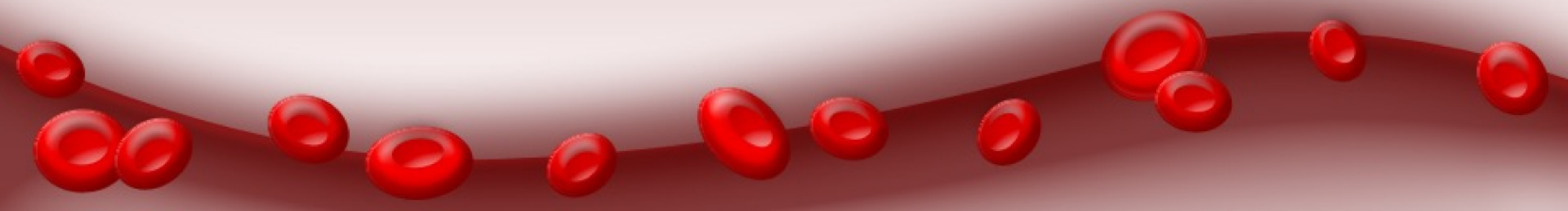
DEFINITIONS:

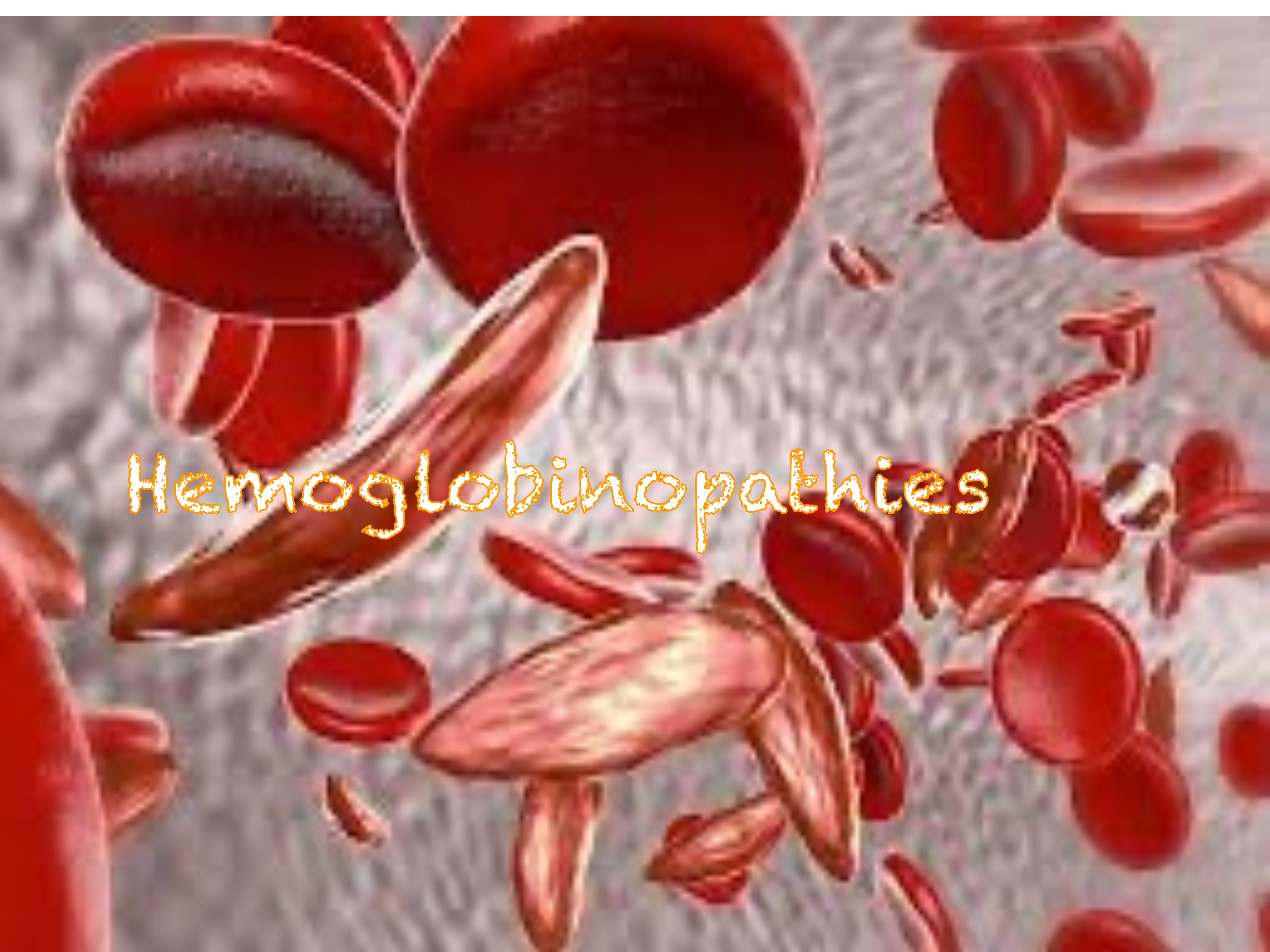
- **Mean cell volume** (MCV)
  - It is the measure of average volume of RBCs
- **Mean cell Hemoglobin** (MCH)
  - It is a measurement of the average weight of hemoglobin in individual erythrocytes.
- **Mean Cell Hemoglobin Concentration** (MCHC)
  - It is the average concentration of hemoglobin in erythrocytes

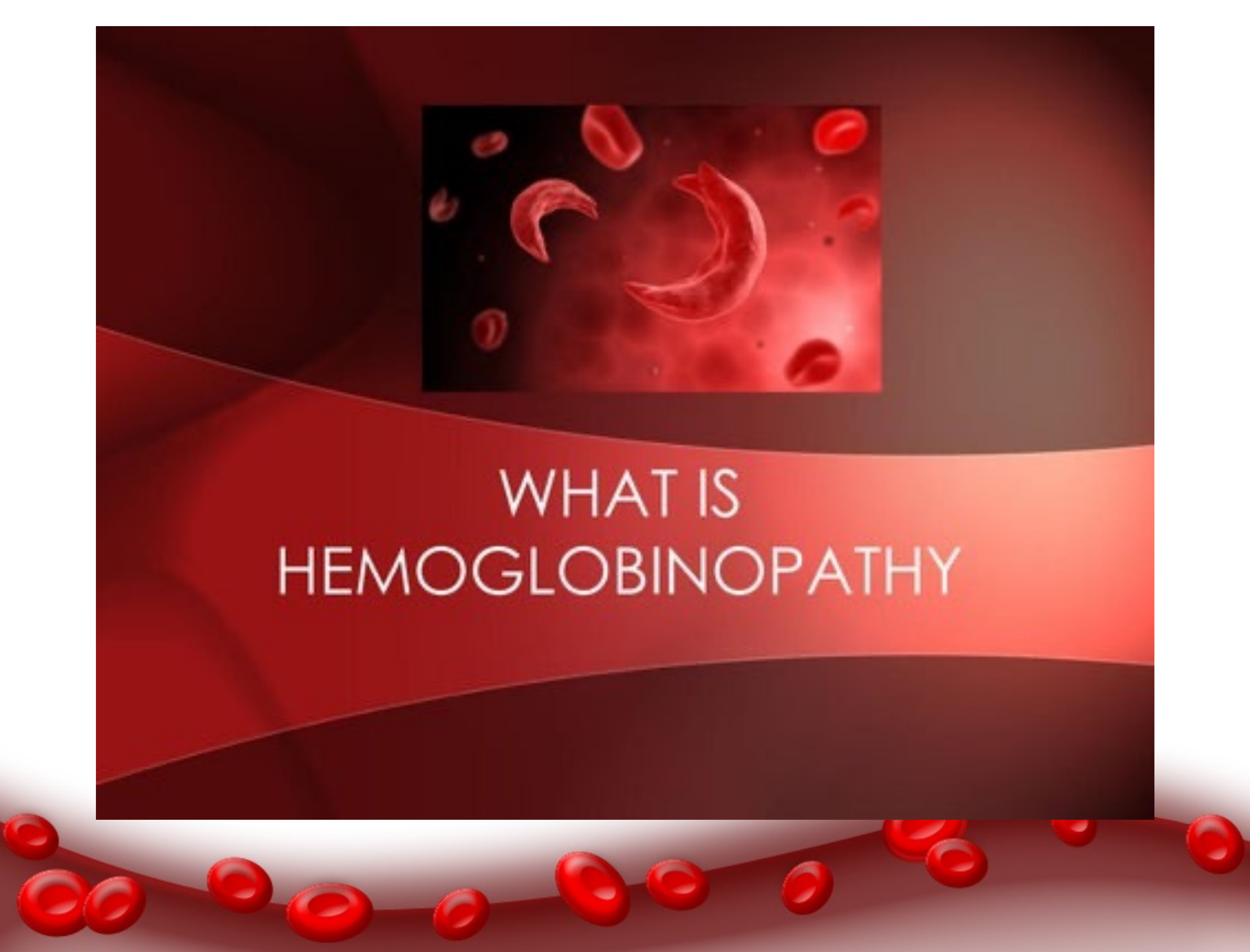
Anemia

There are three types of anemia

	MCV	MCH	MCHC	Disease
1. Normocytic	Normal	Normal	Normal	Aplastic anemia
2.Microcytic hypochromic	Decrease	Decrease	Decrease	Iron deficiency anemia
3.Macrocytic normochromic	Increase	Increase	Normal	Pernicious anemia Foliate deficiency anemia




Hemoglobinopathies


WHAT IS
HEMOGLOBINOPATHY

Hemoglobinopathies

Definition:

- Defects in the globin portion of hemoglobin molecule.
- The defect makes RBCs that contain the abnormal hemoglobin more susceptible to hemolysis.

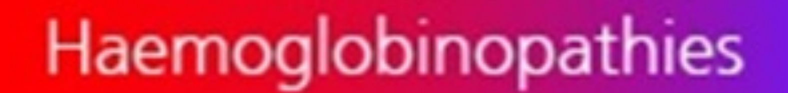
Hemoglobinopathies

- defined as a family of disorders caused either by:

1- production of abnormal hemoglobin molecule
  such as: HbS & HbC

2- Synthesis of insufficient quantities of normal hemoglobin
  such as: thalassemias

3- rarely, both.



Unusual genes that affect the **quality and structure** of haemoglobin

Haemoglobin variants
such as HbS, HbO, HbE

Unusual genes that affect the **quantity** of haemoglobin

Thalassaemias
such as α or β thalassaemia

- **Hemoglobin E** (**HbE**) is an abnormal hemoglobin with a single point mutation in the β chain occurs at high frequencies throughout many Asian countries.

- **Hemoglobin O** (HbO) is a rare type of hemoglobin in which there is a substitution of glutamic acid by lysine as in hemoglobin C, but at different positions.

- **Hemoglobin S** (Hgb S) is an abnormal type of hemoglobin Hemoglobin S is an inherited variant of normal adult hemoglobin (hemoglobin A). It results from a substitution of valine for glutamic acid in the sixth position of the beta (β) globin chain. T



Hemoglobinopathies

Examples:

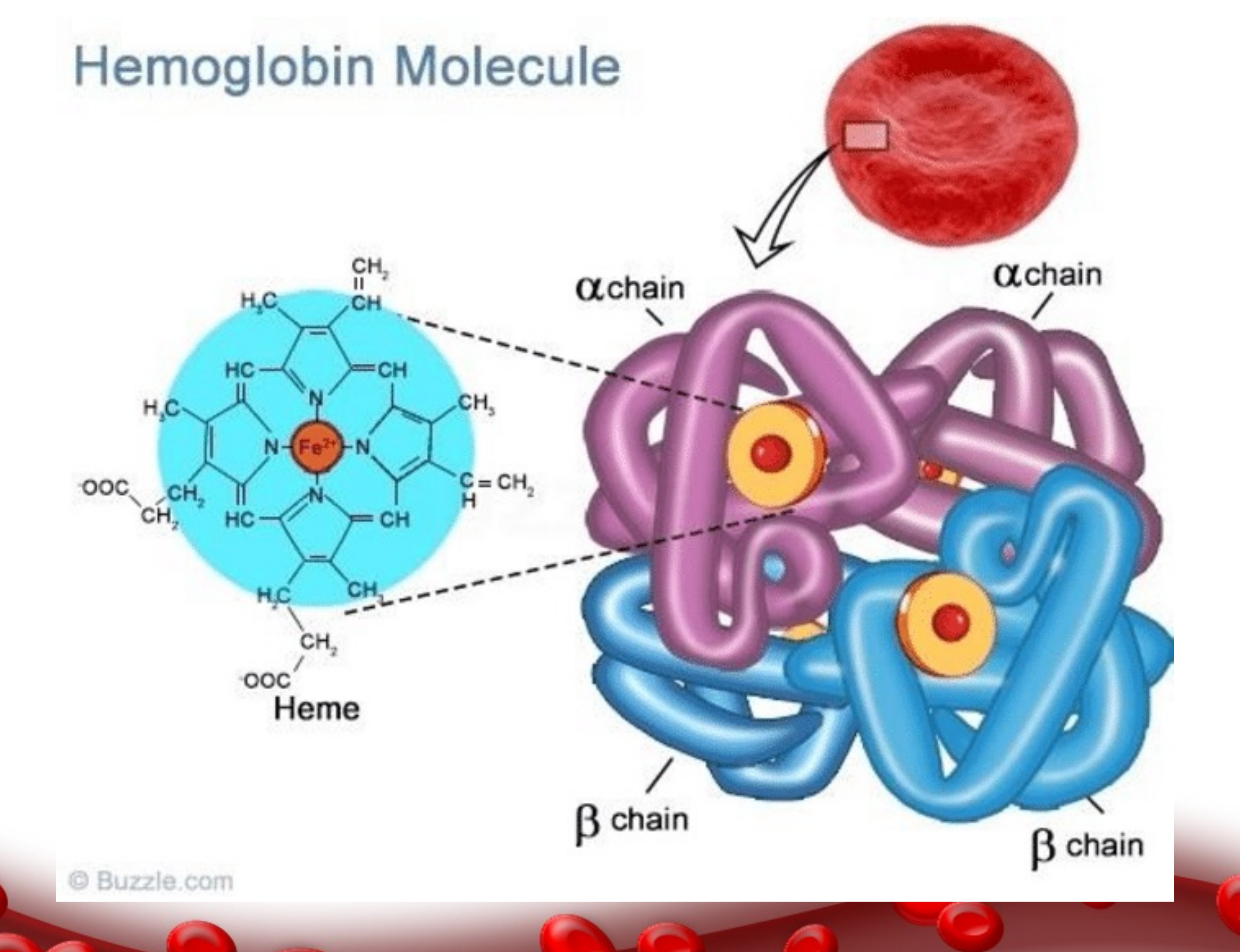
A. Sickle cell disease.

B. Thalassemia

Each hemoglobin molecule consists of two alpha and two beta globin chains bound to a single heme moiety.

Hemoglobinopathies

- Defects of the globin portion of hemoglobin induces the erythrocytes to carry abnormal hemoglobin and the patient is susceptible to hemolytic anemia.
- Adult hemoglobin, Hb A consists of two alpha and two beta globin chains as $\alpha_2 \beta_2$.



Hemoglobin Molecule
Heme
α chain
α chain
β chain
β chain
© Buzzle.com

Hemoglobinopathies

N.B.

- In normal person most of the hemoglobin is HbA.
- At birth about 80% ofhemoglobin is HbF.
- At six months HbF reduced to 5%.
- Adult life HbF is not more than 1%

Hemoglobinopathies

- Fetal hemoglobin, HbF, consists of two alpha and the beta chain are replaced by two gamma chains as α2 δ2.
- Sickle cell disease: involve single amino acid abnormality, the glutamic acid which is normally found in position 6 in beta globin chain is replaced by valine.

Hemoglobinopathies

- **Thalassemia:** characterized by diminished synthesis of the alpha or beta globin chains of hemoglobin.

Sickle Cell Disease

Sickle Cell Disease

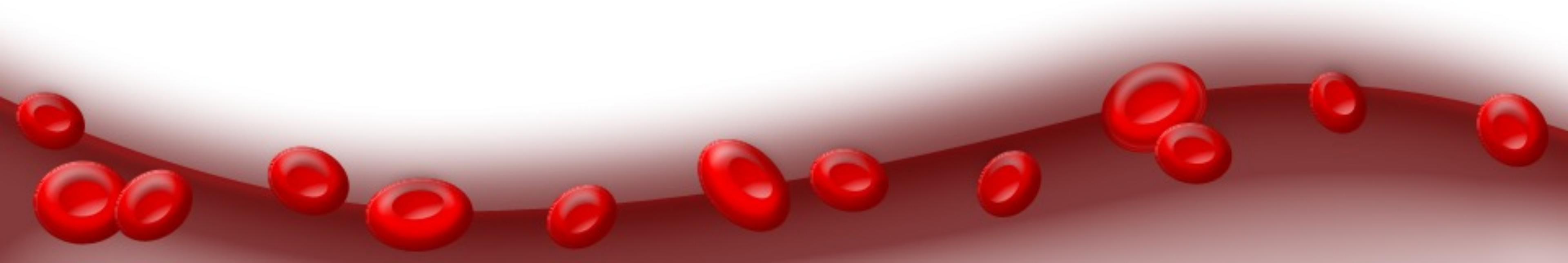
Definition:

- Definition Sickle cell disease is hereditary disorder of hemolytic anemia, characterized by an abnormality in hemoglobin where glutamic acid on beta chain is replaced by valine.

Sickle Cell Disease

The disease may be present in the form of:

- Sickle cell trait.
- Sickle cell anemia.



Pathogenesis

- As a result of this, undesirable physical changes occur in the hemoglobin (HbS). In the presence of either **deoxygenated state or acidosis, the hemoglobin will form sickle-shaped crystal within erythrocyte**, this results in sickling of the RBCs

Sickle Cell Disease

Sickling is precipitated by:

- Infection.
- Dehydration.
- Cold.
- Acidosis.
- Hypoxia (high altitude, general anesthesia).
- In many cases the etiology is unknown.

Sickle Cell Disease

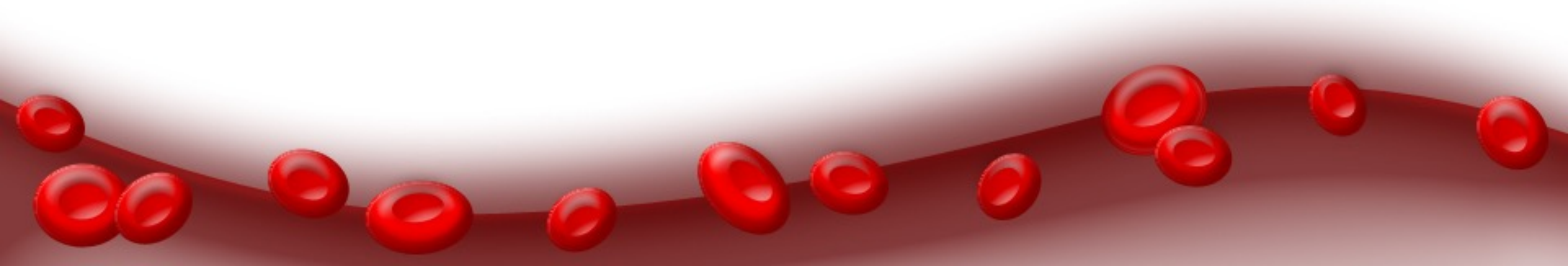
Sickling can lead to:

1. Destruction of sickle cells (hemolysis) with features of anemia.

2. Increased viscosity and clumping of cells in the microcirculation. This leads to thrombosis, ischemia and infarction.

Sickle Cell Disease

Sickle cell trait	Sickle cell anemia
- One beta chain is abnormal	- Two beta chains are abnormal.
- Heterozygous	- Homozygous
- 20%-45% of total Hb is Hb	- 75%-100% of total Hb is HbS.
- The rest of Hb is HbA	- The rest of Hb is HbF.
- No signs or symptoms except under abnormally reduced O_2 tension as general anaesthesia.	- Marked clinical manifestation.



1-Sickle cell anemia

Clinical features:

Extra-oral features:

1. Anemia which may be mild to severe hemolytic anemia. The patient manifests underdevelopment with pallor ,shortness of breath and fatigue
2. **Jaundice:**↑ level of bilirubin due to t hemolysis of RBCs.

Sickle Cell Disease

3. Vasoocclusion:

- Leg → chronic leg ulcers.
- Cerebral vessel → stroke.

4. Crisis:

Painful crisis

- Attack of abdominal pain and bone pain → due to occlusion of blood vessel by ridgid sickled RBC

Aplastic crisis:

- Red blood cell production stops and the patient becomes acutely ill → due to infection.

Sickle Cell Disease

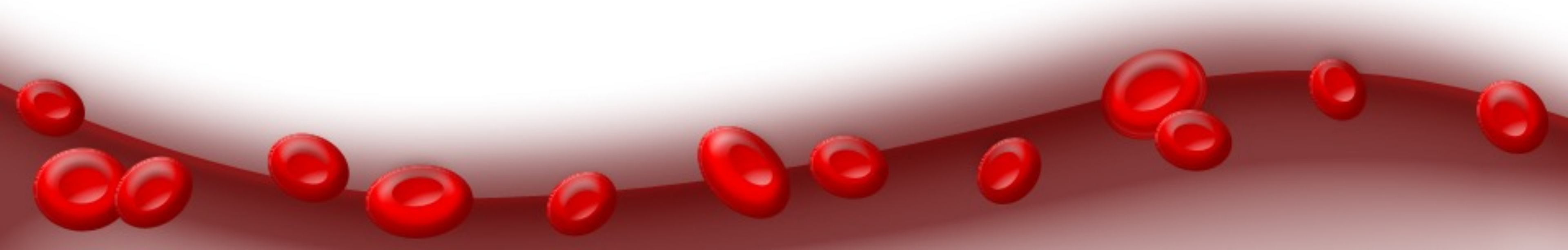
Splenic sequestration crisis

- In early childhood, the spleen is enlarged with entrapment of sickle cells. This can occur acutely in some cases and can be the cause of infant death below one year.
- In adults splenomegaly is rare, due to repeated infarction and fibrosis and functional aplasia occurs in early childhood. Splenic function is lost and te patients are susceptible to infection.

Sickle Cell Disease

Oral manifestations

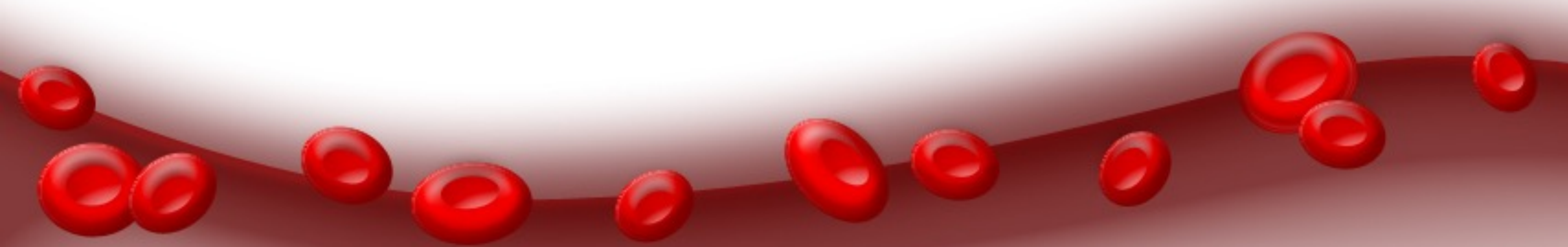
1. The oral mucosa especially the soft palate is pale and has yellowish tinge.
2. Delayed eruption and enamel hypoplasia may be seen.
3. Maxillary over growth







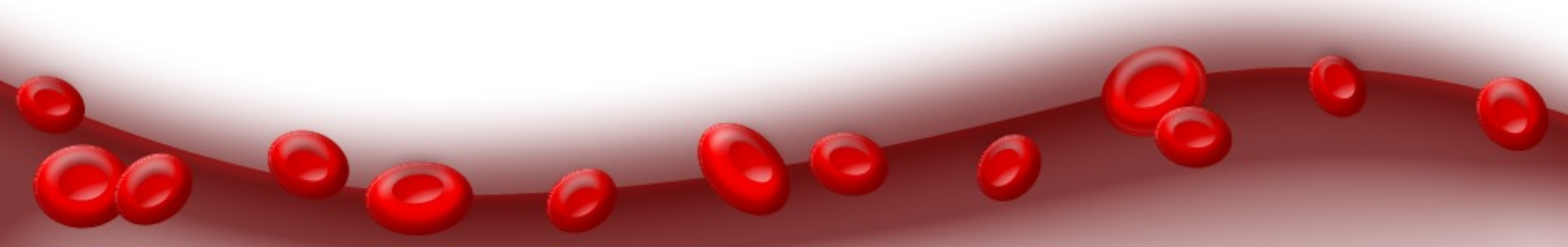




Radiologic changes

1. The jaw bone shows both osteoporosis as well as areas of osteosclerosis.

- The bone changes can be produced by two opposing mechanisms:



Sickle Cell Disease

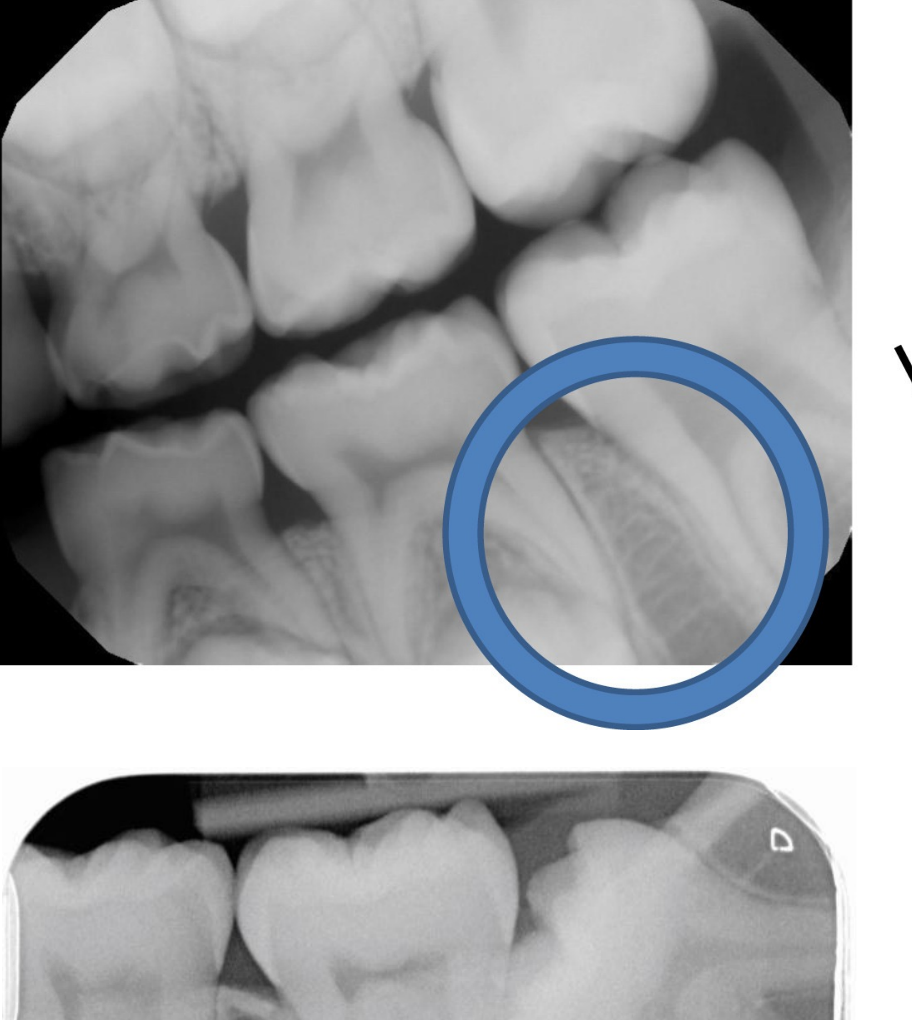
A. Because of the chronic increased erythropoietic activity and marrow hyperplasia, which are attempts to compensate for the hemolysis, osteoporosis occurs.

B. As a result of thrombosis occurring in the capillaries of the bone marrow by sickled cells, thrombosis acts as a nidus for calcification resulting in osteosclerosis. There is osteoporosis and osteosclerosis affecting the mandible, maxilla, skull, vertebrae and long bones.

Sickle Cell Disease

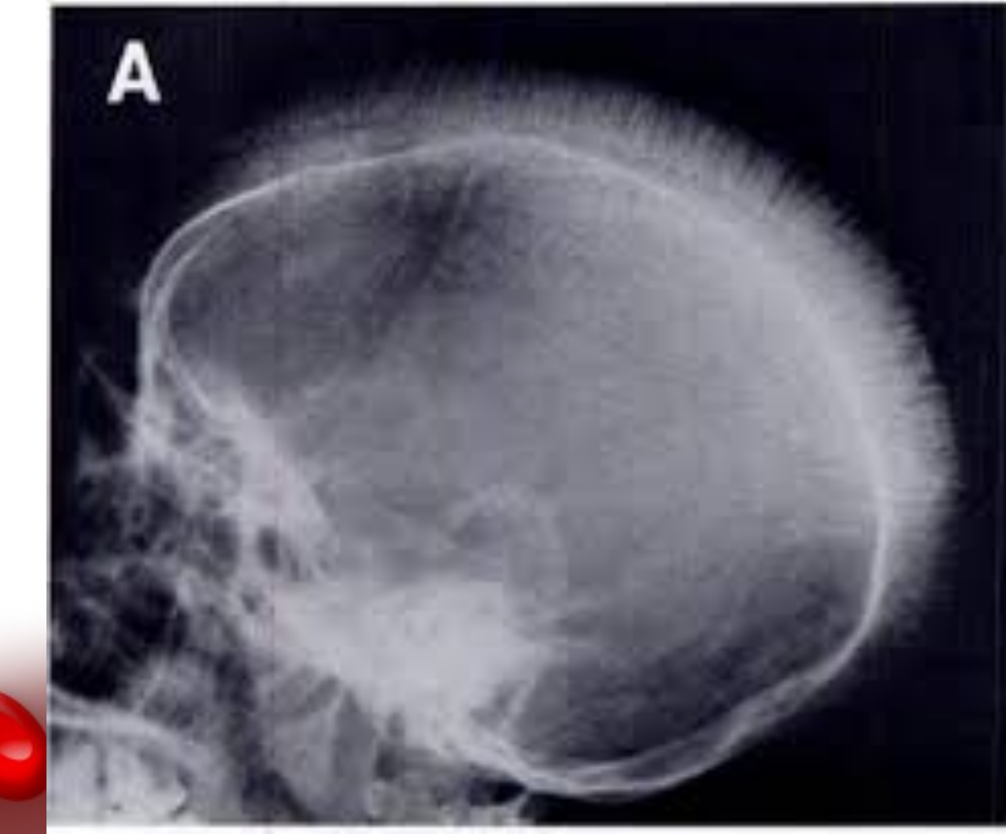
2) The trabecular pattern of alveolar bone tends to run horizontally between the roots of teeth. (Ladder like effect). Lamina dura appears dense and distinct.

3) ***Skull x rays:*** the diploe is thickened (due to bone marrow hyperplasia) and the trabeculae are coarse and tend to run perpendicular to the inner and outer table giving "hair on end appearance". The frontal bossing is very prominent.








A

Sickle Cell Disease

Laboratory findings

1. Normochromic normocytic anemia.

2. Sickling occurs after sealing fresh blood in a small chamber of microscopic side with a reducing agent for 1 hour (sodium metabisulphite).

Sickle Cell Disease

3. ***Sickling solubility test:*** a mixture of Hb S in reducing solution (sodium dithionite) gives a turbid appearance due to precipitation of Hb S, while Hb A, gives clear solution.

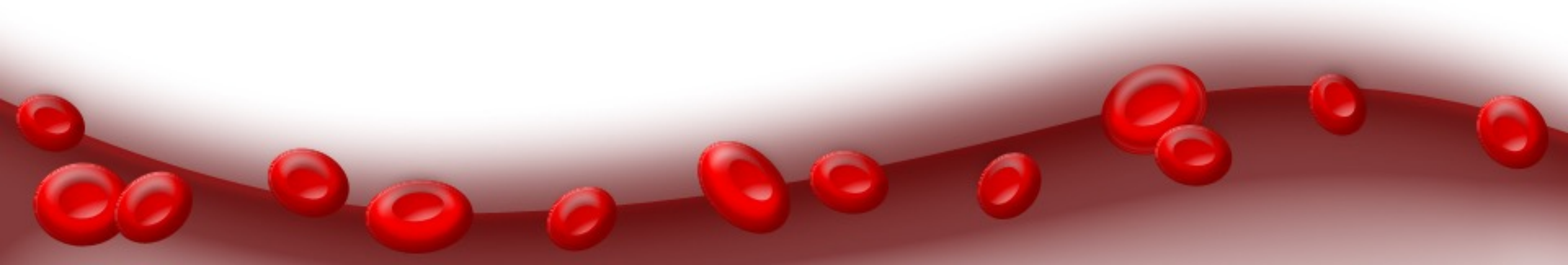
4. Hemoglobin electrophoresis is more accurate methods for the diagnosis. 80%90% is Hb S, the remainder is Hb F.

Sickle Cell Disease

Management

(There is no treatment other than symptomatic treatment).

- The precipitating factors for crises should be avoided.
- No treatment is required for steady state of anemia.



Sickle Cell Disease

- Acute attack requires supportive therapy (IV fluid, oxygen, antibiotic and narcotic analgesic).
- Folic acid given during pregnancy and those with severe hemolysis.
- Blood transfusion is indicated during aplastic crisis were Hb level IS extremely

Sickle Cell Disease

Dental implications:

- Avoid extensive soft tissue surgery due to delayed healing.
- Avoid general anaesthesia as it may result in crisis.
- Treat infection immediately as it may result in aplastic crisis.
- Pain may be due to pulpitis or osteomyelitis secondary to vascular occlusion.

Sickle Cell Disease

2-Sickle cell trait (HbAS)

- This occurs in heterozygous cases in which 60% of hemoglobin is HbsS, the remainder is normal hemoglobin. The patient is asymptomatic and lives nonnallife unaffected by his abnormal hemoglobin. Sickle cell crisis can be caused by reduced oxygen tension (general anesthesia, high altitude or unpressurized aircraft). These patients have few problems in management, but if general anesthesia is necessary full oxygen must be maintained.

Thalassemia

Thalassemia

- Thalassemia (Greek thalassa = sea) are anemia originally found in people living on the shore of the Mediterranean but are now known to affect persons throughout the world.

Definition:

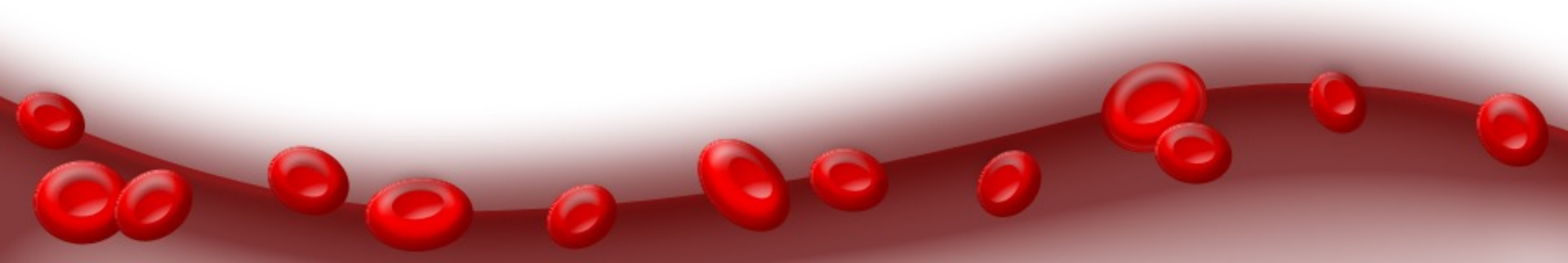
- Group of heredietary diseases characterized by a deficient synthesis of either:

α-chain → α -thalassemia

β-chain → β-thalassemia

Thalassemia

β-thalassemia minor **"β-thalassemia trait"**	**β-thalassemia major** **"Cooley's anemia"**
Heterozygous	Homozygous
Minimal clinical manifestation but genetic counseling is essential.	Clinical manifestation first appears at 4 to 6 months of life (the time of change for Hb from HbF to HbA).

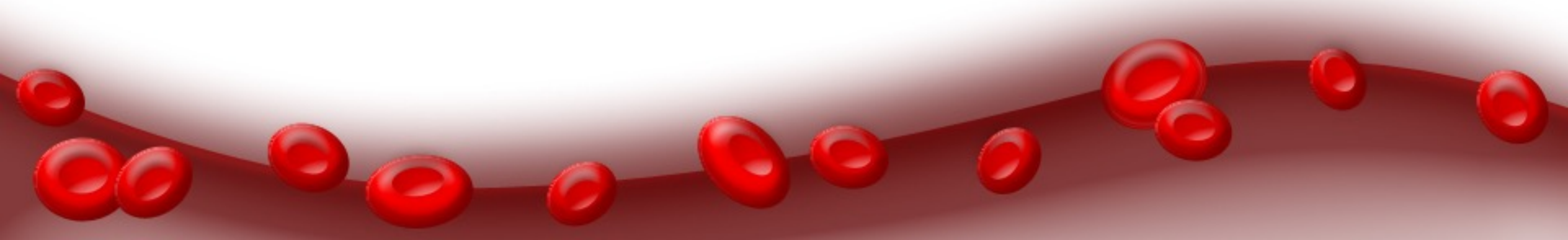


Thalassemia

Clinical features:

Colley's anemia is the most serious type and characterized by:

1. Slow growth & development of children.
2. Ashen gray skin color due to combination pallor, jaundice & hemosiderosis
3. Recurrent bacterial infection (increased availability of iron for bacterial growth).
4. Features of severe anemia.



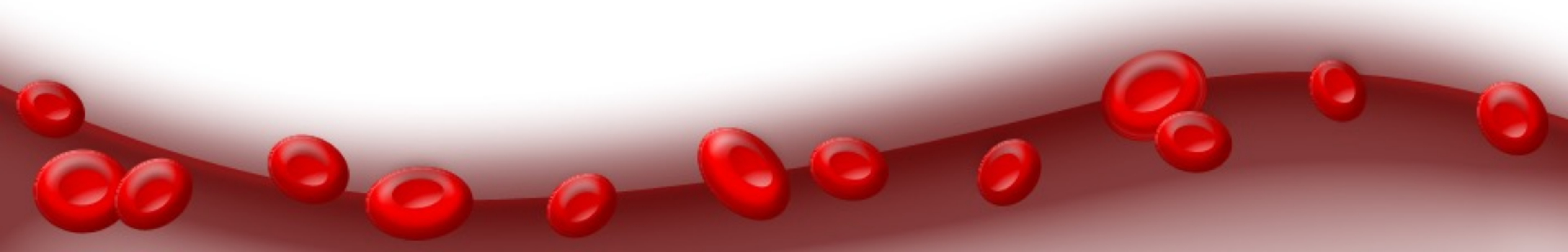
Thalassemia

5. Iron overload; due to:

- Destruction of RBCs with t release of iron.
- Repeated blood transfusion.
- Iron is deposited in heart, liver, pancreas and skin resulting in organ dysfunction.

6. Hepatospleenomegaly

7. .Skeletal growth retardation



Thalassemia

Oral manifestation

1) Oral mucosa appears pale with yellowish tinge because of chronic jaundice, which is best seen at the junction of the hard and soft palate and in the floor of the mouth.

2) Painful swelling of the parotid glands, possibly caused by Iron deposition.

Thalassemia

3) Painful tongue as the patients is susceptible to folate deficiency (as in other chronic hemolytic anemia).

4) Thalassemic face "***Chipmunk face*":**

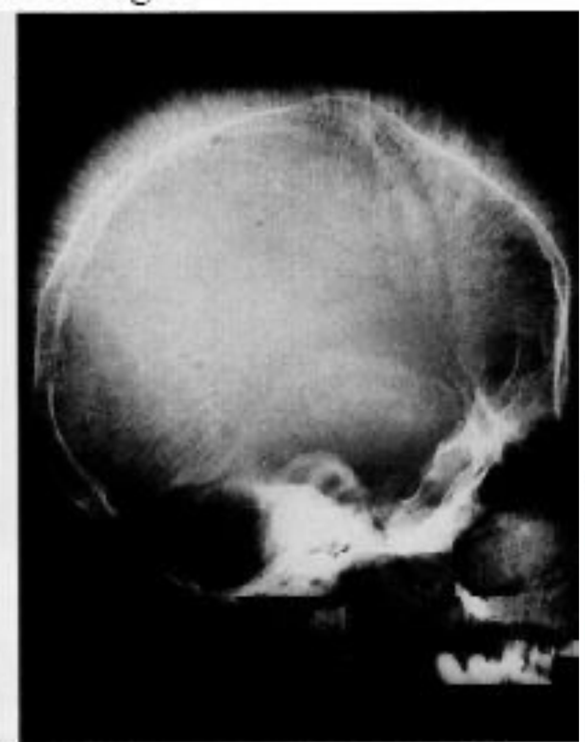
Thalassemia

Hyperplasia of the bone marrow results in the following clinical features:

- Bimaxillary protrusion.
- Retractred upper lip.
- Spacing of teeth.
- Open bite.

Beta Thalassemia Major – bone changes









Thalassemia

5) Dentin and enamel contain excessive amount of iron (5 times normal) with teeth discoloration.

6) Poor wound healing.

Thalassemia

Radiographic features

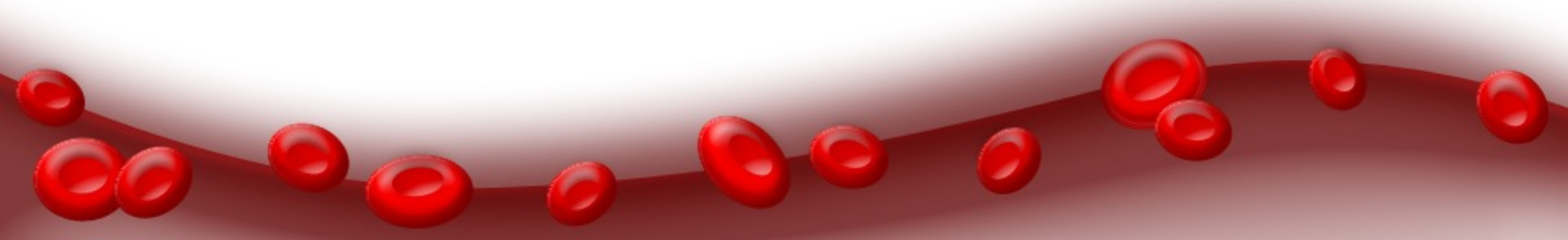
- Similar to sickle cell anemia, but chicken wire appearance of alveolar bone.

LT

A

B

C



Thalassemia

Diagnosis:

1) ↓ RBCs count, Hb concentration.
2) ↓ MCH, MCHC, MCV.
3) Normal serum iron level (to be differentiated from iron deficiency anemia).
4) Electrophoresis: shows ↑ HbF and the remainder is HbA2 (2 alpha chains, 2 delta chains).

Dental Implications

1. Avoid excessive bleeding during surgery
2. Antibiotic prophylaxis is required to control infection especially in splenectomized patients
3. Delayed wound healing is expected.
4. GA is challenging because of enlarged maxilla (difficult intubation)


تعبى وشقايا عند ربنا